Hanley
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STRUCTURE FILE UPDATES:   28 MAY  99  HIGHEST RN 223764-44-1
DICTIONARY FILE UPDATES:  03 JUN  99  HIGHEST RN 223764-44-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 13, 1999

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

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L5              STR
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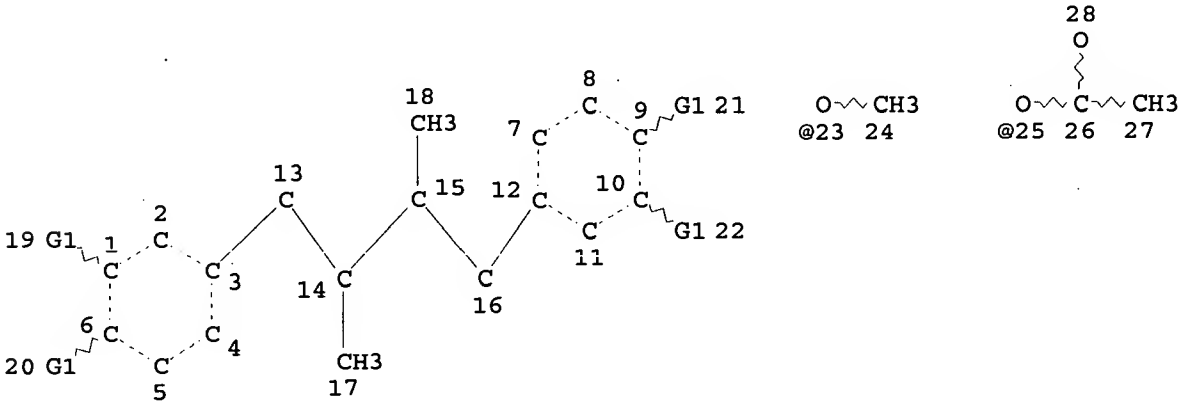


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STEREO ATTRIBUTES: NONE
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Searcher : Shears 308-4994

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      16251359 1/NC
L8          147 L7 AND 1/NC

=> d his l9- ful; sel hit l12 1-29 rn

     (FILE 'CAPLUS' ENTERED AT 16:48:52 ON 03 JUN 1999)
L9         1063 SEA ABB=ON  PLU=ON  L8 OR L8/D
L10           6 SEA ABB=ON  PLU=ON  L9 AND (VIR?(3A)GROW? OR (HSV OR
                HV)(S)HERPES? OR HERPES?)
L11          28 SEA ABB=ON  PLU=ON  L9 AND (ANTIVIR? OR VIRAL? OR
                VIRUS?)
L12          29 SEA ABB=ON  PLU=ON  L10 OR L11

E1 THROUGH E37 ASSIGNED

=> d 1-29 ibib abs hitstr; fil reg

L12  ANSWER 1 OF 29  CAPLUS  COPYRIGHT 1999 ACS
ACCESSION NUMBER:         1999:244515  CAPLUS
DOCUMENT NUMBER:          130:276777
TITLE:                    Nontoxic extract of Larrea tridentata,
                          production method, and therapeutic use
INVENTOR(S):              Sinnott, Robert A.
PATENT ASSIGNEE(S):       Larreacorp, Ltd., USA
SOURCE:                   PCT Int. Appl., 58 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
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     WO 9917609         A1   19990415      WO 98-US19817    19980914
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             DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP,
             KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
             MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,
             TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG,
             KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     WO 9815184         A1   19980416      WO 97-US18103    19971007
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NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW

PRIORITY APPLN. INFO.:

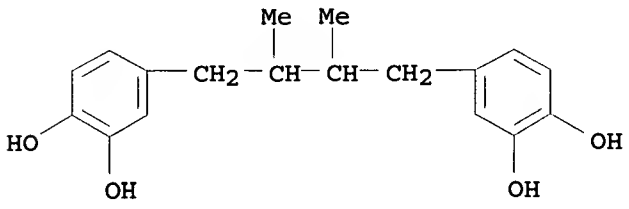
WO 97-US18103	19971007
US 97-64674	19971020
US 97-64802	19971020
US 97-64803	19971020
US 97-64804	19971020
US 97-64805	19971020
US 96-726686	19961007

AB A nontoxic, therapeutic agent having pharmacol. activity comprising concd. ext. of Larrea tridentata plant material and ascorbic acid is made by a process in which the plant material is extd. using an org. solvent, and is then satd. with ascorbic acid to reduce the toxic NDGA quinone, which naturally occurs in the plant material, to NDGA itself. Addnl. amts. of ascorbic acid are added to the ext. to inhibit the natural oxidn. of the NDGA into the toxic NDGA quinone in vivo, or during processing or storage. The resulting ext. is useful in the treatment of **viral** diseases caused by **viruses** from the **Herpesviridae** family or **viruses** which require the Sp1 class of proteins to initiate **viral** replications. The resulting compd. can also be used as an antiinflammatory when the inflammatory diseases are mediated by the effects of leukotrienes. The listed reducing agents can also be used to stabilize NDGA as a therapeutic agent or a food additive.

IT **500-38-9P**, Nordihydroguaiaretic acid
RL: BAC (Biological activity or effector, except adverse); FFD (Food or feed use); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Larrea tridentata nontoxic ext., prodn. method, combinations with other agents, and therapeutic use)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)

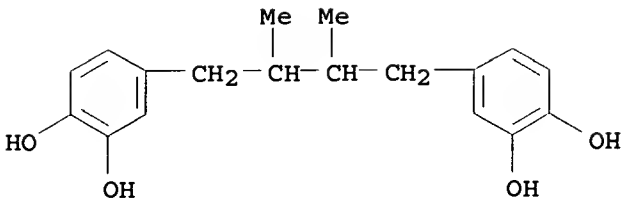


IT **500-38-9D**, Nordihydroguaiaretic acid, oxidn. products
RL: RCT (Reactant)
(Larrea tridentata nontoxic ext., prodn. method, combinations with other agents, and therapeutic use)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA

INDEX NAME)



L12 ANSWER 2 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1998:601918 CAPLUS
DOCUMENT NUMBER: 129:310451
TITLE: Human immunodeficiency **virus** type 1 cDNA integration: new aromatic hydroxylated inhibitors and studies of the inhibition mechanism
AUTHOR(S): Farnet, C. M.; Wang, B.; Hansen, M.; Lipford, J. R.; Zalkow, L.; Robinson, W. E., Jr.; Siegel, J.; Bushman, F.
CORPORATE SOURCE: Salk Institute for Biological Studies, La Jolla, CA, 92037, USA
SOURCE: Antimicrob. Agents Chemother. (1998), 42(9), 2245-2253
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

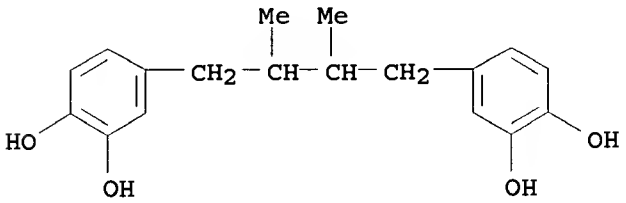
AB Integration of the HIV-1 cDNA is a required step for **viral** replication. Integrase, the **virus**-encoded enzyme important for integration, was not yet exploited as a target for clin. useful inhibitors. Here we report on the identification of new polyhydroxylated arom. inhibitors of integrase including ellagic acid, purpurogallin, 4,8,12-trioxatricornan, and hypericin, the last of which is known to inhibit **viral** replication. These compds. and others were characterized in assays with subviral preintegration complexes (PICs) isolated from HIV-1-infected cells. Hypericin was found to inhibit PIC assays, while the other compds. tested were inactive. Counterscreening of these and other integrase inhibitors against addnl. DNA-modifying enzymes revealed that none of the polyhydroxylated arom. compds. are active against enzymes that do not require metals (methylases, a pox **virus** topoisomerase). However, all were cross-reactive with metal-requiring enzymes (restriction enzymes, a reverse transcriptase), implicating metal atoms in the inhibitory mechanism. In mechanistic studies, we localized binding of some inhibitors to the catalytic domain of integrase by assaying competition of binding

by labeled nucleotides. These findings help elucidate the mechanism of action of the polyhydroxylated arom. inhibitors and provide practical guidance for further inhibitor development.

IT **500-38-9**, Nordihydroguaiaretic acid
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(inhibition activity and mechanism of arom. hydroxylated inhibitors for HIV-1 cDNA integration tested on preintegration complexes)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 3 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1998:484927 CAPLUS

DOCUMENT NUMBER: 129:127177

TITLE: Pharmaceutical preparations of glutathione and methods of administration

INVENTOR(S): Demopoulos, Harry B.; Seligman, Myron L.

PATENT ASSIGNEE(S): Antioxidant Pharmaceuticals Corp., USA

SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9829101	A1	19980709	WO 97-US23879	19971231
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9856205	A1	19980731	AU 98-56205	19971231

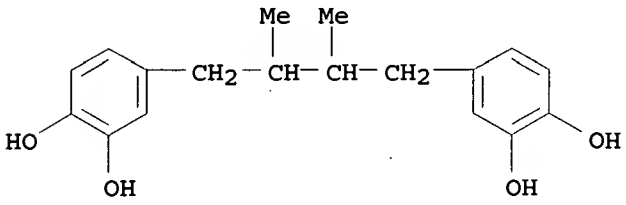
PRIORITY APPLN. INFO.: US 96-34101 19961231
WO 97-US23879 19971231

AB A method of increasing glutathione levels in mammalian cells comprises administering an oral bolus of encapsulated pharmaceutically stabilized glutathione in a rapidly dissolving formulation to a mammal on an empty stomach. Pharmaceutical formulations including glutathione are also disclosed.

IT **500-38-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (glutathione pharmaceutical prepns. and methods of administration)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 4 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1998:450910 CAPLUS
DOCUMENT NUMBER: 129:197598
TITLE: **Antiviral** Activities of Methylated Nordihydroguaiaretic Acids. 2. Targeting **Herpes** Simplex **Virus** Replication by the Mutation Insensitive Transcription Inhibitor Tetra-O-methyl-NDGA
AUTHOR(S): Chen, Hongshan; Teng, Li; Li, Jian-Nong; Park, Richard; Mold, David E.; Gnabre, John; Hwu, Jih Ru; Tseng, Wen Nan; Huang, Ru Chih C.
CORPORATE SOURCE: Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences, Beijing, Peop. Rep. China
SOURCE: J. Med. Chem. (1998), 41(16), 3001-3007
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We had previously reported that tetramethyl-O-NGDA (M4N), a synthetic deriv. of the naturally occurring nordihydroguaiaretic acid (NDGA), is able to inhibit HIV Tat transactivation by blocking host Sp1 protein at the Sp1 cognate binding site on the HIV LTR promoter. The present studies were undertaken to examine whether

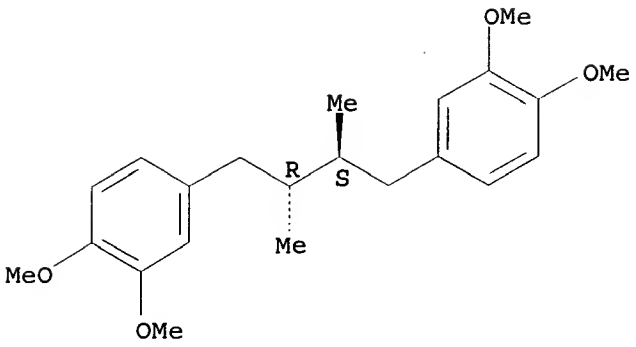
M4N is able to inhibit the replication of **herpes** simplex **virus** (**HSV**), another Sp1-regulated **virus** . The results showed that in Vero cells, M4N inhibits at micromolar levels (IC50 = 43.5 .mu.M) the expression of the **herpes** immediate early gene (.alpha.-ICP4), which is essential for **HSV** replication. An electrophoretic mobility shift assay, examg. Sp1 binding to the .alpha.-ICP4 promoter, showed a significant inhibition of the control bands: 88% inhibition of the fast moving band (FMB) and 45% of the slow moving band (SMB), at 100 .mu.M of drug concn. Comparative studies between M4N and acycloguanosine (acyclovir, ACV) in cultured Vero cells revealed an interesting pattern in the drug sensitivity (IC50) and cytotoxicity (TC50) parameters. For M4N, the IC50 varied between 11.7 and 4 .mu.M in 10 passages of HSV-1 and 4 passages of HSV-2 with no indication for a requirement of higher drug concn. In contrast, for acyclovir, the IC50 increased from 7 .mu.M in the first passage to 444 .mu.M in the tenth passage of HSV-1, and >88 .mu.M for the fourth passage of HSV-2, indicating a rapid build-up of drug resistance against acyclovir. While the selective index (SI), defined as the ratio: TC50/IC50, remained relatively const. for M4N; it dropped 60-fold for acyclovir in the endpoints of **viral** passages. Drug sensitivity for M4N toward the acyclovir-sensitive strain (sm44) and the acyclovir-resistant strain (ACV-10) of HSV-1 was similar, indicating no cross-resistance between M4N and acyclovir in their anti-HSV effects. These results may have an important clin. relevance since HSV has been shown to be a factor for spreading of HIV.

IT **24150-24-1**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting **herpes** simplex **virus** replication by mutation-insensitive transcription inhibitor tetra-O-methyl-NDGA)

RN 24150-24-1 CAPLUS

CN Benzene, 1,1'-(2,3-dimethyl-1,4-butanediyl)bis[3,4-dimethoxy-, (R*,S*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L12 ANSWER 5 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1998:450908 CAPLUS
DOCUMENT NUMBER: 129:216452
TITLE: **Antiviral** Activities of Methylated Nordihydroguaiaretic Acids. 1. Synthesis, Structure Identification, and Inhibition of Tat-Regulated HIV Transactivation
AUTHOR(S): Hwu, Jih Ru; Tseng, Wen Nan; Gnabre, John; Giza, Paul; Huang, Ru Chih C.
CORPORATE SOURCE: Organosilicon and Synthesis Laboratory Department of Chemistry, National Tsing Hua University, Hsinchu, 30043, Taiwan
SOURCE: J. Med. Chem. (1998), 41(16), 2994-3000
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:216452
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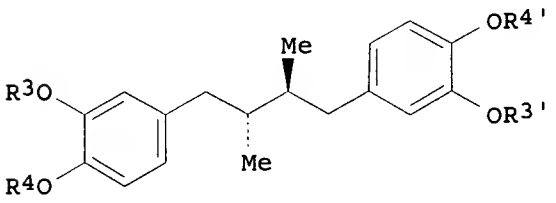


I

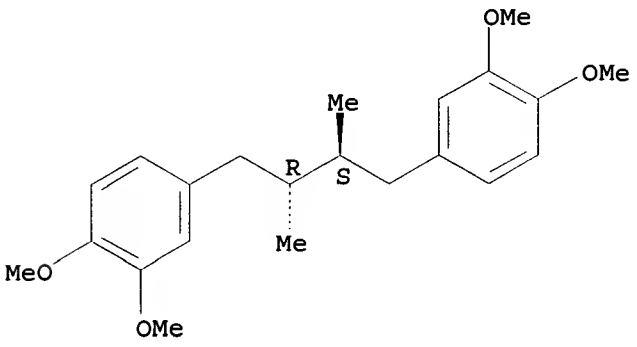
AB Treatment of meso-nordihydroguaiaretic acid (NDGA) I (R3 = R4 = R3' = R4' = H) with 0.50-4.1 equiv of di-Me sulfate and 3.0-6.0 equiv of potassium carbonate in acetone at 56 .degree.C gave nine methylated products. Eight of those mono-, di-, tri-, and tetra-O-methylated

NDGAs were isolated in pure form, and their structures were identified unambiguously by spectroscopic methods. A preparative amt. of tetra-Me NDGA I (R3 = R4 = R3' = R4' = Me) was obtained in 99% yield from NDGA by use of 4.1 equiv of di-Me sulfate for the methylation. Among the eight different methylated NDGAs, I (R3 = R4 = R3' = R4' = Me) showed the strongest anti-HIV activity (IC50 11 .mu.M). Chem. synthesized 3-O-methyl-NDGA I (R3 = Me, R4 = R3' = R4' = H) showed identical anti-HIV activity (IC50 25 .mu.M) to the lignan isolated from Creosote Bush. Lignans with methylated catecholic hydroxyl groups can be produced in large quantities with low cost. At drug concns. below 30 .mu.M, I (R3 = R4 = R3' = R4' = Me) was a stronger anti-HIV agent than mono- and dimethylated NDGAs.

IT **24150-24-1P 66322-34-7P 71113-15-0P**
171204-38-9P 171204-39-0P 171439-76-2P
212325-18-3P 212325-19-4P
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis, structure, and inhibition of Tat-regulated HIV transactivation of **antiviral** methylated nordihydroguaiaretic acids)

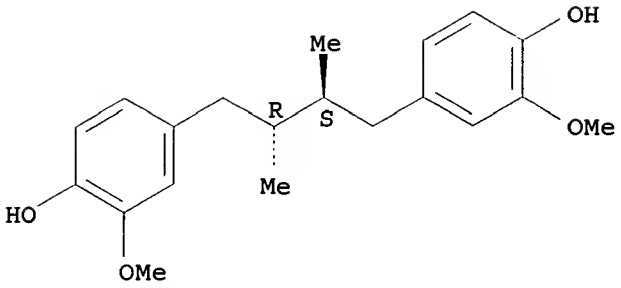
RN 24150-24-1 CAPLUS
CN Benzene, 1,1'-(2,3-dimethyl-1,4-butanediyl)bis[3,4-dimethoxy-, (R*,S*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



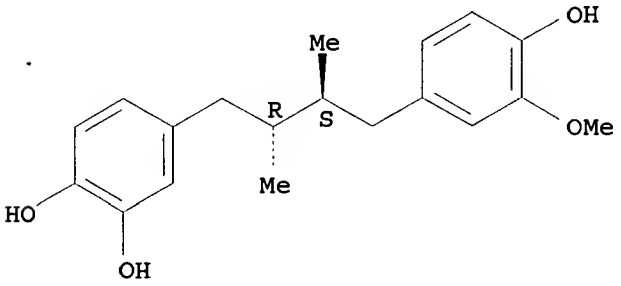
RN 66322-34-7 CAPLUS
CN Phenol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis[2-methoxy-, (R*,S*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



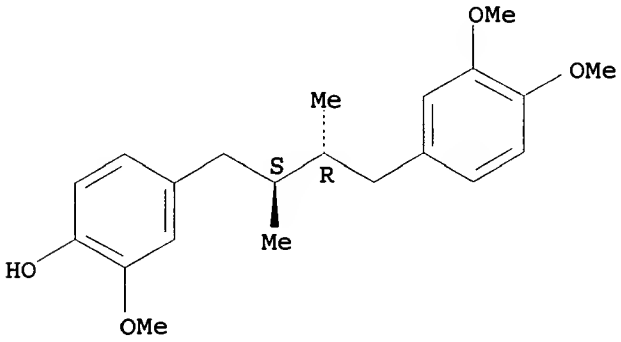
RN 71113-15-0 CAPLUS
CN 1,2-Benzenediol, 4-[(2R,3S)-4-(4-hydroxy-3-methoxyphenyl)-2,3-dimethylbutyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 171204-38-9 CAPLUS
CN Phenol, 4-[(2R,3S)-4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, rel- (9CI) (CA INDEX NAME)

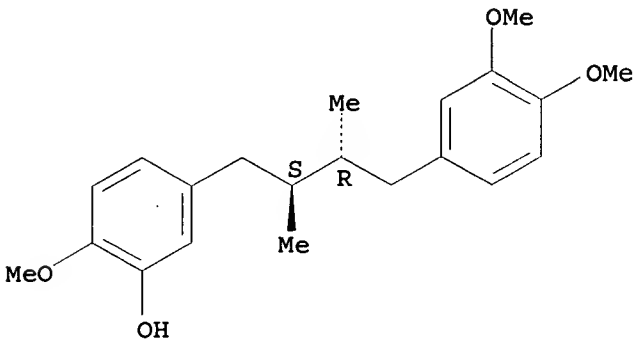
Relative stereochemistry.



RN 171204-39-0 CAPLUS

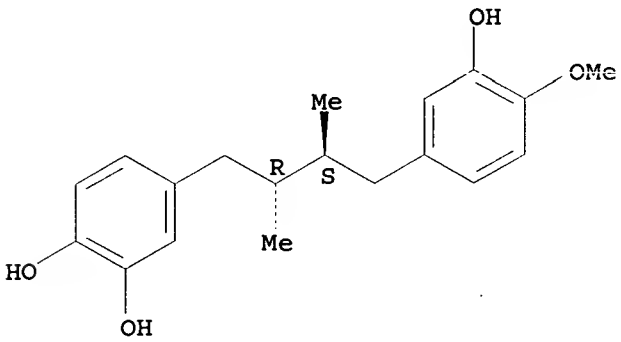
CN Phenol, 5-[(2R,3S)-4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 171439-76-2 CAPLUS
CN 1,2-Benzenediol, 4-[(2R,3S)-4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 212325-18-3 CAPLUS
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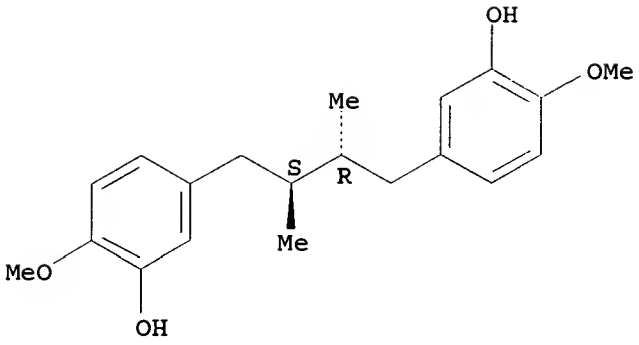
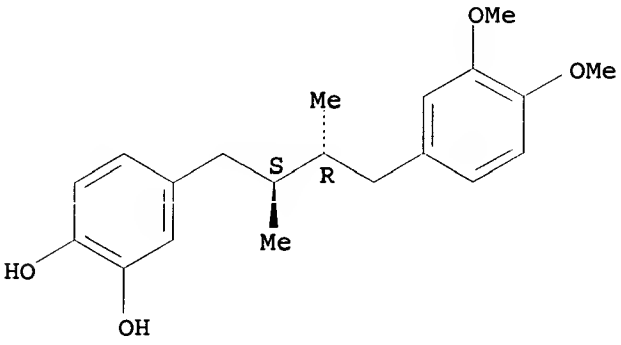
Relative stereochemistry.



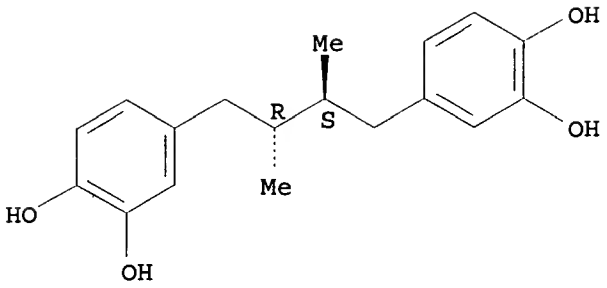
RN 212325-19-4 CAPLUS
CN 1,2-Benzenediol, 4-[(2R,3S)-4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



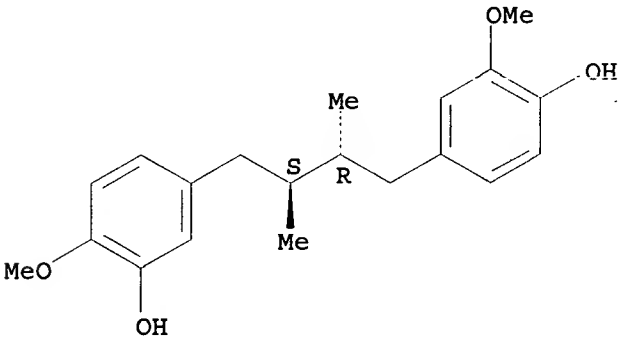
IT **27686-84-6**, meso-Nordihydroguaiaretic acid
RL: PRP (Properties); RCT (Reactant)
(synthesis, structure, and inhibition of Tat-regulated HIV transactivation of **antiviral** methylated nordihydroguaiaretic acids)
RN 27686-84-6 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis-, (R*,S*)-(9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **171204-43-6P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(synthesis, structure, and inhibition of Tat-regulated HIV transactivation of **antiviral** methylated nordihydroguaiaretic acids)
RN 171204-43-6 CAPLUS
CN Phenol, 4-[(2R,3S)-4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L12 ANSWER 6 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1998:341491 CAPLUS
DOCUMENT NUMBER: 129:12742
TITLE: Methods and compositions using thalidomide or other angiogenesis-inhibitory compound and anti-inflammatory agent for inhibition of angiogenesis
INVENTOR(S): D'Amato, Robert J.
PATENT ASSIGNEE(S): Children's Medical Center, USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
Searcher : Shears 308-4994

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9819649	A2	19980514	WO 97-US20116	19971104
WO 9819649	A3	19980625		

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

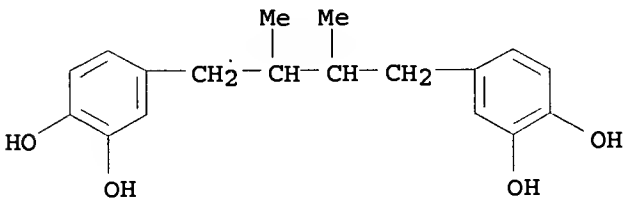
AU 9851973	A1	19980529	AU 98-51973	19971104
PRIORITY APPLN. INFO.:			US 96-28708	19961105
			US 97-963058	19971103
			WO 97-US20116	19971104

OTHER SOURCE(S): MARPAT 129:12742

AB A group of compds. that effectively inhibit angiogenesis is provided. More specifically, thalidomide and various related compds.,e.g. thalidomide precursors, analogs, metabolites and hydrolysis products, have been shown to inhibit angiogenesis and to treat disease states resulting from angiogenesis. Addnl., antiinflammatory drugs, such as steroids and NSAIDs can inhibit angiogenesis-dependent diseases either alone or in combination with thalidomide and related compds. Importantly, these compds. can be administered orally.

IT **500-38-9**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thalidomide or other angiogenesis-inhibitory compd. and anti-inflammatory agent for inhibition of angiogenesis)

RN 500-38-9 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



Searcher : Shears 308-4994

L12 ANSWER 7 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1998:289269 CAPLUS
DOCUMENT NUMBER: 129:52663
TITLE: Retrograde trafficking of both Golgi complex and TGN markers to the ER induced by nordihydroguaiaretic acid and cyclofenil diphenol
AUTHOR(S): Drecktrah, Daniel; De Figueiredo, Paul; Mason, Roger M.; Brown, William J.
CORPORATE SOURCE: Section of Biochemistry, Molecular and Cell Biology, Cornell University, Ithaca, NY, 14853, USA
SOURCE: J. Cell Sci. (1998), 111(7), 951-965
CODEN: JNCSAI; ISSN: 0021-9533
PUBLISHER: Company of Biologists Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

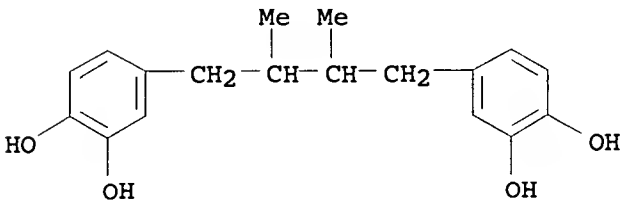
AB Previous studies have shown that the Golgi stack and the trans-Golgi network (TGN) may play a role in capturing escaped resident endoplasmic reticulum (ER) proteins, and directing their retrograde transport back to that organelle. Whether this retrograde movement represents a highly specific or more generalized membrane trafficking pathway is unclear. To better understand both the retrograde and anterograde trafficking pathways of the secretory app., the in vivo effects of two structurally unrelated compds., the potent lipoxygenase inhibitor nordihydroguaiaretic acid (NDGA), and the non-steroidal estrogen cyclofenil diphenol (CFD), both of which are known to inhibit secretion, were examd. In the presence of these compds., transport of vesicular stomatitis **virus** G membrane glycoprotein from the ER to the Golgi complex, and from the TGN to the cell surface, was inhibited potently and rapidly. It was found that NDGA and CFD stimulated the rapid, but not concomitant, retrograde movement of both Golgi stack and TGN membrane proteins back to the ER until both organelles were morphol. absent from cells. Both NDGA- and CFD-stimulated TGN and Golgi retrograde membrane trafficking were inhibited by microtubule depolymg. agents and energy poisons. Removal of NDGA and CFD resulted in the complete, but not concomitant, reformation of both Golgi stacks and their closely assocd. TGN compartments. These studies suggest that NDGA and CFD unmask a generalized bulk recycling pathway to the ER for both Golgi and TGN membranes and, further, that NDGA and CFD are useful for investigating the mol. mechanisms that control the formation and maintenance of both the Golgi stack proper and the TGN.

IT **500-38-9**, Nordihydroguaiaretic acid
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(retrograde trafficking of both Golgi complex and TGN markers to

the endoplasmic reticulum induced by nordihydroguaiaretic acid and cyclofenil diphenol)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 8 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1998:239082 CAPLUS

DOCUMENT NUMBER: 128:275069

TITLE: Nontoxic therapeutic extract of Larrea tridentata

INVENTOR(S): Sinnott, Robert A.; Clark, Dennis W.; De Boer, Kenneth Frank

PATENT ASSIGNEE(S): LarreaCorp, Ltd., USA; Sinnott, Robert A.; Clark, Dennis W.; De Boer, Kenneth Frank

SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9815184	A1	19980416	WO 97-US18103	19971007
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
US 5837252	A	19981117	US 96-726686	19961007
AU 9748956	A1	19980505	AU 97-48956	19971007
WO 9917609	A1	19990415	WO 98-US19817	19980914
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

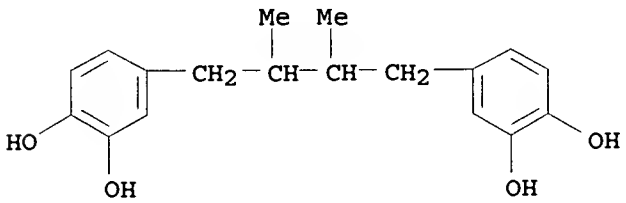
US 96-726686	19961007
WO 97-US18103	19971007
US 97-64674	19971020
US 97-64802	19971020
US 97-64803	19971020
US 97-64804	19971020
US 97-64805	19971020

AB A nontoxic, therapeutic agent having pharmacol. activity comprising concd. ext. of Larrea tridentata and a reducing agent, such as ascorbic acid, an ascorbic acid ester, an ascorbic acid salt, butylated hydroxyanisole, butylated hydroxytoluene, hydrogen sulfide, hypophosphorous acid, monothioglycerol, potassium bisulfite, Pr gallate, sodium bisulfite, sodium hydrosulfite, sodium thiosulfate, sulfur dioxide, sulfurous acid, a tocopherol, or vitamin E. The active principle is nordihydroguaiaretic acid (NDGA). The plant material is extd. using an org. solvent, preferably acetone, and is then satd. with one of the listed reducing agents to reduce the toxic NDGA quinone, which naturally occurs in the plant material, to NDGA itself. Addnl. amts. of reducing agent may be added to the ext. to inhibit the natural oxidn. of the NDGA into the toxic NDGA quinone in vivo, or during processing or storage. The resulting ext. is useful in the treatment of **viral** diseases caused by **viruses** from the **Herpesviridae** family or **viruses** which require the Sp1 class of proteins to initiate **viral** replications. The resulting compd. can also be used as an anti-inflammatory agent when the inflammatory diseases are mediated by the effects of leukotrienes. The listed reducing agents can also be used to stabilize NDGA as a therapeutic agent or a food additive.

IT **500-38-9P**, Nordihydroguaiaretic acid
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(active principle in therapeutic ext. of Larrea tridentata)

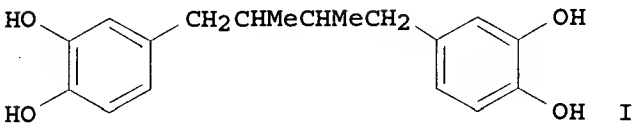
RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



Searcher : Shears 308-4994

L12 ANSWER 9 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1998:163109 CAPLUS
DOCUMENT NUMBER: 128:280435
TITLE: Purification of anti-HIV lignans from Larrea tridentata by pH-zone-refining countercurrent chromatography
AUTHOR(S): Ma, Y.; Qi, L.; Gnabre, J. N.; Huang, R. C. C.; Chou, F. E.; Ito, Y.
CORPORATE SOURCE: Laboratory of Biomedical Chemistry, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, 20892-1676, USA
SOURCE: J. Liq. Chromatogr. Relat. Technol. (1998), 21(1 & 2), 171-181
CODEN: JLCTFC; ISSN: 1082-6076
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

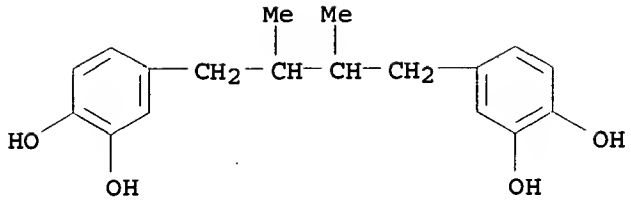


I

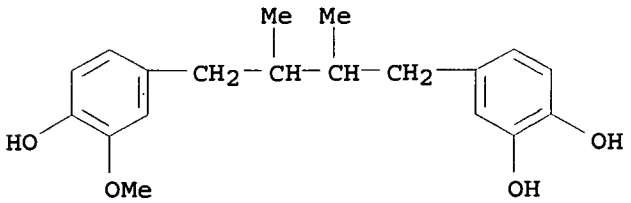
AB Anti-HIV lignans were purified from ext. of Larrea tridentata by high-speed countercurrent chromatog. (CCC) using pH-zone-refining CCC. When a column filled with Me t-Bu ether, contg. trifluoroacetic acid at 25 mM, was eluted with aq. NaOH, 10 to 20 g of the crude ext. was sepd. into NDGA (I) and its monomethyl esters rectangular peaks assocd. with their specific pH (pH zones). The method was also successfully applied to synthetic lignans, resulting in resoln. of NDGA and its mono and di-Me esters.

IT **500-38-9P**, NDGA **54473-24-4P 178557-46-5P 205758-62-9P**
RL: PUR (Purification or recovery); PREP (Preparation)
(purifn. of anti-HIV lignans from Larrea tridentata by pH-zone-refining countercurrent chromatog.)

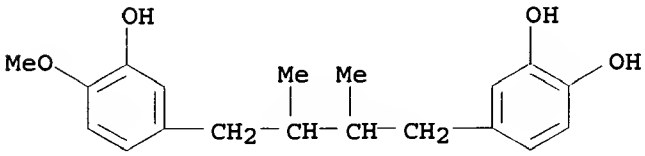
RN 500-38-9 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



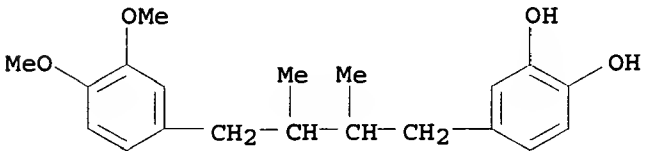
RN 54473-24-4 CAPLUS
CN 1,2-Benzenediol, 4-[4-(4-hydroxy-3-methoxyphenyl)-2,3-dimethylbutyl]-
(9CI) (CA INDEX NAME)



RN 178557-46-5 CAPLUS
CN 1,2-Benzenediol, 4-[4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-
(9CI) (CA INDEX NAME)

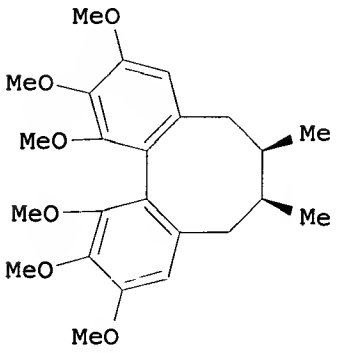


RN 205758-62-9 CAPLUS
CN 1,2-Benzenediol, 4-[4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-
(9CI) (CA INDEX NAME)



L12 ANSWER 10 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1997:536638 CAPLUS
Searcher : Shears 308-4994

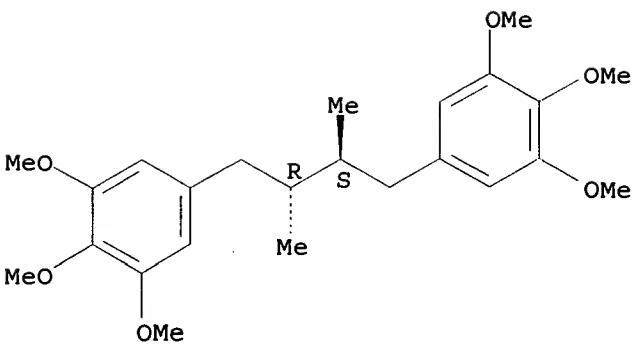
DOCUMENT NUMBER: 127:190585
TITLE: A new synthesis method for (.+-.)-deoxyschizandrin
AUTHOR(S): Wu, Anxin; Zhao, Yurui; Qin, Binchang; Chen, Ning; Pan, Xinfu
CORPORATE SOURCE: State Key Laboratory of Applied Organic Chemistry, Department of Chemistry, Lanzhou University, Lanzhou, 730000, Peop. Rep. China
SOURCE: Chin. Sci. Bull. (1997), 42(12), 995-998
CODEN: CSBUEF; ISSN: 1001-6538
PUBLISHER: Science Press
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Deoxyschizandrin (I) isolated from Schizandra chinensis exhibits antihepatitis **virus** activity. Interest in the synthesis of I comes from its bioactivity. A new very efficient route to the synthesis of (.+-.)-deoxyschizandrin via gallic acid in 10 steps with the overall yield of 12% and using the I2/NaOEt oxidative coupling reaction as a key step is described.
IT **72730-20-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(new method for the prepn. of (.+-.)-deoxyschizandrin)
RN 72730-20-2 CAPLUS
CN Benzene, 1,1'-(2,3-dimethyl-1,4-butanediyl)bis[3,4,5-trimethoxy-, (R*,S*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L12 ANSWER 11 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1997:332397 CAPLUS
DOCUMENT NUMBER: 126:301796
TITLE: Use of 2-mercaptoethanolamine (2-MEA) and related aminothiol compounds and copper(II)-3,5 diisopropyl salicylates and related compounds in the prevention and treatment of AIDS, cancer, autoimmune disease, microbiological infections, and other diseases
INVENTOR(S): Chachoua, Samir
PATENT ASSIGNEE(S): Chachoua, Samir, Mex.
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9711666	A2	19970403	WO 96-IB1059	19960925
WO 9711666	A3	19970619		
W: AL, AM, AU, BB, BG, BR, CA, CN, CU, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2233015	AA	19970403	CA 96-2233015	19960925
CA 2233445	AA	19970403	CA 96-2233445	19960925
AU 9669990	A1	19970417	AU 96-69990	19960925
EP 858327	A2	19980819	EP 96-931214	19960925
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

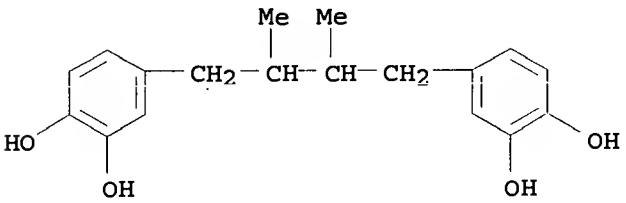
PRIORITY APPLN. INFO.: US 95-4281 19950925
WO 96-IB1059 19960925

AB New therapeutic compns. and applications of 2-MEA and related aminothiols and copper(II)-3,5-diisopropyl salicylates, solely or in combination with other factors, agents, or processes that are phys., chem. and/or biol.-based, are disclosed. These include precursors, intermediates, end products, catalysts, promoters and/or any factors, agents, or processes involved directly or indirectly from initial application of the compns. to the final result. The methods and compns. of the invention are useful for the treatment of AIDS, cancer, autoimmune disease, and microbiol. infections, as well as other diseases in which immunol. dysfunction and/or free radical formation function as part of the disease mechanism.

IT **500-38-9**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mercaptoethanolamine, related aminothiols, copper diisopropyl salicylate, and related compds., alone or in combination, for prevention and treatment of disease)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 12 OF 29 CAPLUS COPYRIGHT 1999 ACS

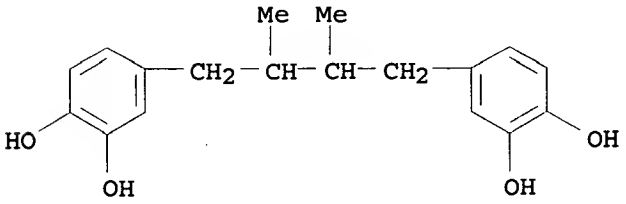
ACCESSION NUMBER: 1997:142788 CAPLUS
DOCUMENT NUMBER: 126:224234
TITLE: Activation of the NF-KB transcription factor in a T-lymphocytic cell line by hypochlorous acid
AUTHOR(S): Schoonbroodt, Sonia; Legrand-Poels, Sylvie; Best-Belpomme, Martin; Piette, Jacques
CORPORATE SOURCE: Laboratory of Virology, institute of Pathology B23, University of Liege, Liege, B-4000, Belg.
SOURCE: Biochem. J. (1997), 321(3), 777-785
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Reactive oxygen species (ROS) such as hydrogen peroxide serve as second messengers in the induction of the transcription factor

NF-.kappa.B, and hence in the activation and replication of human immunodeficiency **virus** type 1 (HIV-1) in human cells. During inflammatory reactions, many oxidative species are produced, one of which is hypochlorous acid (HOCl), which is responsible for the microbicidal effects of activated human polymorphonuclear leukocytes. Treatment of a T-lymphocytic cell line with micromolar concns. of HOCl promoted the appearance of transcription factor NF-.kappa.B (the heterodimer p50/p65) in the nucleus of the cells, even in the absence of de novo protein synthesis. Western blot anal. of the NF-.kappa.B inhibitory subunits (I.kappa.B) demonstrated that both I.kappa.B-.alpha. proteolysis and p105 processing were induced by the treatment. NF-.kappa.B activation was very effective when cells were subjected to hyperthermia before being treated with HOCl. Various antioxidants, such as pyrrolidine dithiocarbamate, p-bromophenacyl-bromide and nordihydroguaiaretic acid could strongly reduce NF-.kappa.B translocation, demonstrating the importance of oxidative species in the transduction mechanism. Moreover, ACH-2 cells treated with HOCl or H2O2 released tumor necrosis factor-.alpha. (TNF-.alpha.) in the supernatants. The importance of TNF-.alpha. release in NF-.kappa.B induction by HOCl or H2O2 was demonstrated by the fact that: (1) the nuclear appearance of NF-.kappa.B was promoted in untreated cells; and (2) synergism between TNF-.alpha. and HOCl was detected. Collectively, these results suggest that HOCl should be considered as an oxidative species capable of inducing NF-.kappa.B in a T-lymphocytic cell line through a transduction mechanism involving ROS, and having a long-distance effect through subsequent TNF-.alpha. release.

IT **500-38-9**, Nordihydroguaiaretic acid
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(activation of the NF-KB transcription factor in a T-lymphocytic cell line by hypochlorous acid response to)

RN 500-38-9 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 13 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1996:425306 CAPLUS
DOCUMENT NUMBER: 125:76343

TITLE: Nordihydroguaiaretic acid derivatives for the suppression of HIV Tat transactivation

INVENTOR(S): Huang, Ru Chih; Gnabbe, John N.
PATENT ASSIGNEE(S): Johns-Hopkins University, USA

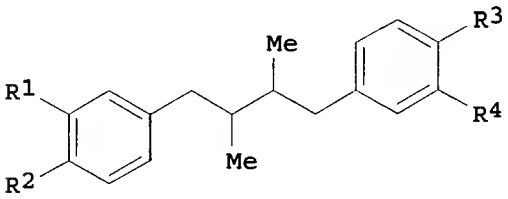
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9610549	A1	19960411	WO 95-US11779	19950922
W: AU, CA, CN, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2200991	AA	19960411	CA 95-2200991	19950922
AU 9536339	A1	19960426	AU 95-36339	19950922
AU 700481	B2	19990107		
EP 783474	A1	19970716	EP 95-933830	19950922
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1162301	A	19971015	CN 95-196035	19950922
JP 10509421	T2	19980914	JP 95-511844	19950922
US 5663209	A	19970902	US 96-627588	19960404
PRIORITY APPLN. INFO.:			US 94-316341	19940930
			WO 95-US11779	19950922

OTHER SOURCE(S): MARPAT 125:76343

GI



I

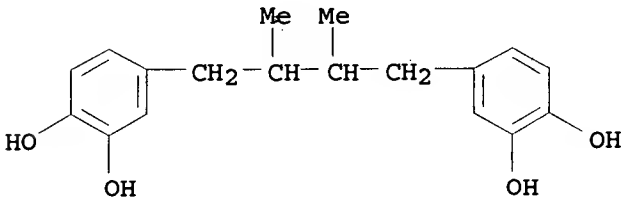
AB The invention reveals the isolation, purifn. and characterization from the creosote bush Larrea tridentata of compds. I [R1-R4 = OH, OMe, CH3C(O)O, provided that R1-R4 are not each OH simultaneously]. Each compd. is a deriv. of 1,4-bis(3,4-dihydroxyphenyl)-2,3-dimethylbutane (nordihydroguaiaretic acid, NDGA). In addn., NDGA and each deriv. can be used in a method to suppress Tat transactivation of a lentivirus, including the HIV **virus**, in a cell by administering NDGA or a deriv. of NDGA to the cell.

Searcher : Shears 308-4994

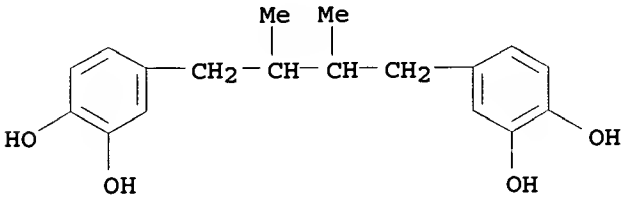
Fractionation of NDGA derivs. from Larrea tridentata is described. Inhibition of transactivation of HIV promoter activity by NDGA and 4-O-methyl-NDGA was detd.

IT **500-38-9DP**, Nordihydroguaiaretic acid, derivs.
500-38-9P, Nordihydroguaiaretic acid **178557-46-5P**
RL: BAC (Biological activity or effector, except adverse); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nordihydroguaiaretic acid derivs. from Larrea tridentata for suppression of Tat transactivation of HIV or other lentivirus)

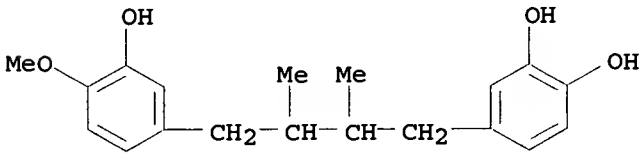
RN 500-38-9 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



RN 500-38-9 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



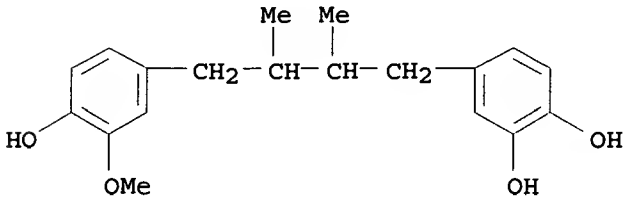
RN 178557-46-5 CAPLUS
CN 1,2-Benzenediol, 4-[4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]- (9CI) (CA INDEX NAME)



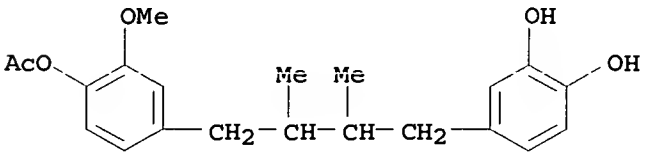
IT **54473-24-4P 178557-47-6P 178557-48-7P**

178557-49-8P 178557-50-1P 178557-51-2P
178557-52-3P 178557-53-4P
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nordihydroguaiaretic acid derivs. from Larrea tridentata for suppression of Tat transactivation of HIV or other lentivirus)

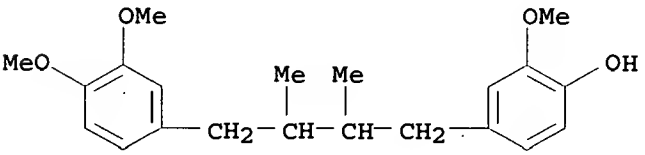
RN 54473-24-4 CAPLUS
CN 1,2-Benzenediol, 4-[4-(4-hydroxy-3-methoxyphenyl)-2,3-dimethylbutyl]- (9CI) (CA INDEX NAME)



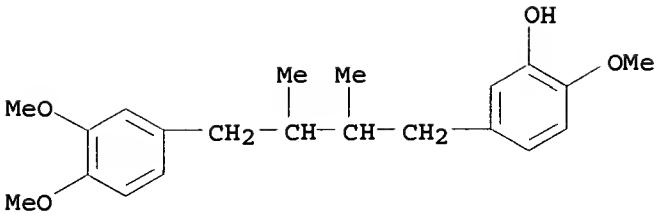
RN 178557-47-6 CAPLUS
CN 1,2-Benzenediol, 4-[4-[4-(acetyloxy)-3-methoxyphenyl]-2,3-dimethylbutyl]- (9CI) (CA INDEX NAME)



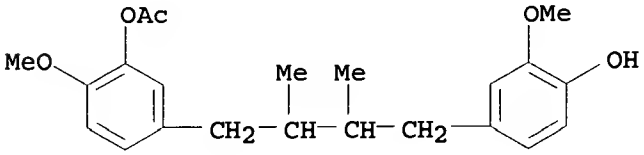
RN 178557-48-7 CAPLUS
CN Phenol, 4-[4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-methoxy- (9CI) (CA INDEX NAME)



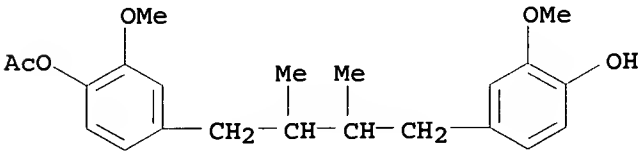
RN 178557-49-8 CAPLUS
CN Phenol, 5-[4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-methoxy- (9CI) (CA INDEX NAME)



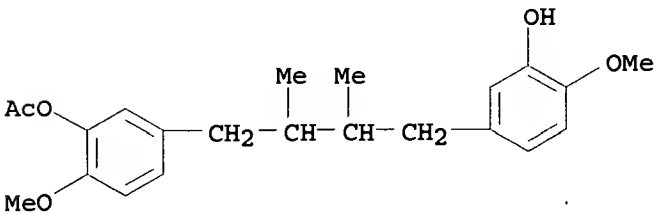
RN 178557-50-1 CAPLUS
CN Phenol, 4-[4-[3-(acetyloxy)-4-methoxyphenyl]-2,3-dimethylbutyl]-2-methoxy- (9CI) (CA INDEX NAME)



RN 178557-51-2 CAPLUS
CN Phenol, 4-[4-[4-(acetyloxy)-3-methoxyphenyl]-2,3-dimethylbutyl]-2-methoxy- (9CI) (CA INDEX NAME)

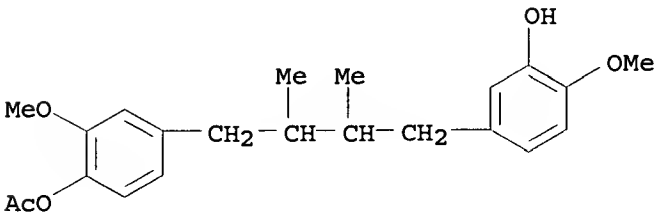


RN 178557-52-3 CAPLUS
CN Phenol, 5-[4-[3-(acetyloxy)-4-methoxyphenyl]-2,3-dimethylbutyl]-2-methoxy- (9CI) (CA INDEX NAME)



RN 178557-53-4 CAPLUS

CN Phenol, 4-[4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, 1-acetate (9CI) (CA INDEX NAME)

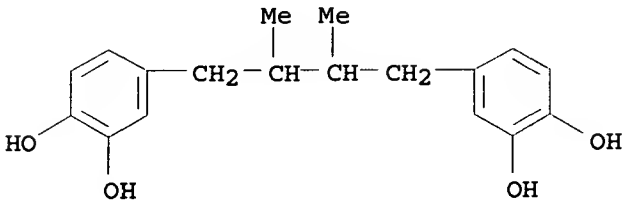


L12 ANSWER 14 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1996:371202 CAPLUS
DOCUMENT NUMBER: 125:54332
TITLE: Inhibition of vesicle-mediated protein transport by nordihydroguaiaretic acid
AUTHOR(S): Tagaya, Mitsuo; Henomatsu, Nobuhiro; Yoshimori, Tamotsu; Yamamoto, Akitsugu; Tashiro, Yutaka; Mizushima, Shoji
CORPORATE SOURCE: Sch. Life Sci., Tokyo Univ. Pharm. Life Sci., Hachioji, 192-03, Japan
SOURCE: J. Biochem. (Tokyo) (1996), 119(5), 863-869
CODEN: JOBIAO; ISSN: 0021-924X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nordihydroguaiaretic acid (NDGA), a phospholipase A2 inhibitor, blocks intra-Golgi protein transport in a cell-free system and prolactin secretion from HG2 cells [Tagaya, M., Henomatsu, N., Yoshimiri, T., Yamamoto, A., Tashiro, Y., and Fukui, T. (1993) FEBS Lett. 324, 201-204]. To det. which intracellular secretory pathway(s) is inhibited by NDGA, we investigated its effect on the transport of the vesicular stomatitis **virus**-encoded glycoprotein in BHK-21 cells. NDGA blocked protein transport from the endoplasmic reticulum to the Golgi app., and from the trans-Golgi network to the plasma membrane. In addn., it retarded the brefeldin A-induced retrograde transport of mannosidase II to the endoplasmic reticulum. Although NDGA had an inhibitory effect on protein synthesis, it induced the expression of BiP, a chaperone located in the endoplasmic reticulum. The induction of BiP may be a consequence of the inhibition of protein transport by NDGA.

IT **500-38-9**, Nordihydroguaiaretic acid
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(inhibition of vesicle-mediated protein transport by nordihydroguaiaretic acid, a phospholipase A2 inhibitor)
RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 15 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1996:309295 CAPLUS
DOCUMENT NUMBER: 125:1316
TITLE: Effects of cellular aging on the induction of c-fos by antioxidant treatments
AUTHOR(S): Keogh, Bart P.; Tresini, Maria; Cristofalo, Vincent J.; Allen, R. G.
CORPORATE SOURCE: Center Gerontological Research, Medical College Pennsylvania, Philadelphia, PA, 19129, USA
SOURCE: Mech. Ageing Dev. (1996), 86(3), 151-160
CODEN: MAGDA3; ISSN: 0047-6374
DOCUMENT TYPE: Journal
LANGUAGE: English

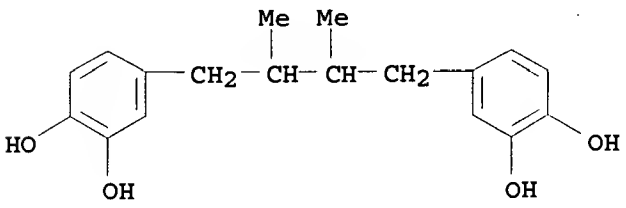
AB The proto-oncogene c-fos (the cellular homolog of v-fos, Finkel-Biskis-Jinkins (FBJ) murine osteogenic sarcoma virus) encodes a major component of the activator protein-1 (AP-1) transcription factor. Serum stimulation as well as oxidizing treatments induce transitory increases in c-fos mRNA abundance. The induction of c-fos by serum stimulation is also known to decline during proliferative senescence. In this study, we examd. the effects of two classes of antioxidants on the induction of c-fos in early and late passage human fetal lung fibroblasts (WI-38). N-acetyl cysteine (NAC) induces c-fos transcription in both early and late passage cells, while nordihydroguaiaretic acid (NGA) induced c-fos transcription in early passage cells but fails to stimulate it in late passage cells. Since we had previously obsd. an age-related decline in protein kinase C (PKC) translocation from the cytosol to the membrane, following its activation, and because PKC activation appears to be involved in the NGA induction of c-fos we examd. the relative protein abundances of several PKC isoforms in early and late passage cells. Addnl., we examd. the protein abundance of several members of the MAP kinase pathway which could play a role in c-fos induction by the PKC-dependent pathway. We were unable to detect PKC-.beta. in early or late passage cells. Late passage cells contained a slightly greater abundance of PKC .alpha., .gamma. and .epsilon. than cells at an early passage. No

other differences in PKC isoforms or in members of the MAP kinase family were obsd. in early or late passage cells. These results clearly demonstrate that at least some pathways leading to c-fos induction remain intact in late passage cells.

IT **500-38-9**, Nordihydroguaiaretic acid
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(effects of cellular aging on induction of c-fos by antioxidant treatments)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 16 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1996:135789 CAPLUS

DOCUMENT NUMBER: 124:167496

TITLE: Enhancement of introduction of foreign matter into higher eukaryotic cells by co-introduction of anti-apoptosis or anti-inflammatory substances

INVENTOR(S): Cotten, Matthew; Baker, Adam; Chiocca, Susanna

PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany

SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9533062	A2	19951207	WO 95-EP1989	19950526
W: AU, BR, CA, CN, JP, KR, MX, PL, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 4418825	A1	19951207	DE 94-4418825	19940530
DE 4442587	A1	19960801	DE 94-4442587	19941130
AU 9526160	A1	19951221	AU 95-26160	19950526
EP 767840	A2	19970416	EP 95-920887	19950526

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

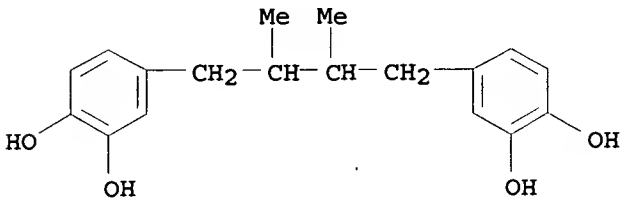
JP 10500578	T2	19980120	JP 95-500282	19950526
PRIORITY APPLN. INFO.:			DE 94-4418825	19940530
			DE 94-4442587	19941130
			WO 95-EP1989	19950526

AB The toxicity problems arising when foreign matter is introduced into higher eukaryotic cells, esp. with transfection with DNA, are obviated by expression in the cell of gene products that block the apoptosis induced by the transfection process and/or by treating the cells with anti-inflammatory substances. Preferred anti-apoptosis genes are Bcl-2, adenovirus E1B 19K or an anti-apoptotic gene of the CELO avian adenovirus. The preferred anti-inflammatory substance is adenovirus VA1, which is introduced into the cell in the form of VA1 DNA. These measures help to achieve a long-lasting gene expression. The anti-apoptotic gene of CELO **virus** was cloned and sequenced. The enhancement by the above genes of mammalian cell transfection using transferrin (or streptavidin)-polylysine conjugate/adenovirus transfection complexes was demonstrated. The synergistic effect of anti-inflammatory compds. such as glucocorticoids, ibuprofen, etc. was also shown.

IT **500-38-9**, NDGA
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(enhancement of introduction of foreign matter into higher eukaryotic cells by co-introduction of anti-apoptosis or anti-inflammatory substances)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 17 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER:	1996:58761 CAPLUS
DOCUMENT NUMBER:	124:211685
TITLE:	Isolation of anti-HIV-1 lignans from Larrea tridentata by counter-current chromatography
AUTHOR(S):	Gnabre, John Noel; Ito, Yoichiro; Ma, Ying; Huang, Ru Chih
CORPORATE SOURCE:	Department of Biology, The Johns Hopkins

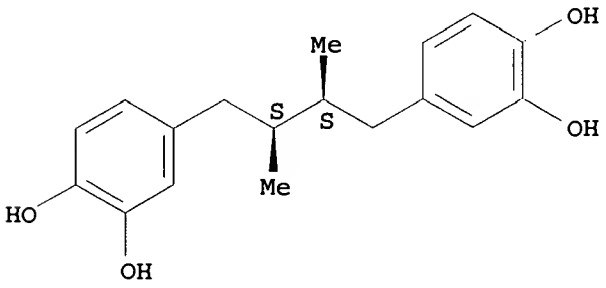
University, 144 Mudd Hall, 3400 N. Charles Street, Baltimore, MD, 21218-2685, USA
SOURCE: J. Chromatogr., A (1996), 719(2), 353-64
CODEN: JCRAEY; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several lignans, mostly new, were isolated from Larrea tridentata by assay-guided counter-current chromatog. (CCC). Using the secreted alk. phosphatase bioassay of HIV Tat transactivation and the 2-phase hexane-Et acetate-methanol-water solvent system, 2 major components (Gr and Lo) were identified as anti-HIV active principles. The chem. structures of the constituents of Gr (G1-G4) and Lo (L1-L4) were detd. by GC-MS and NMR. After optimization of isolation conditions, a large-scale isolation with the chloroform-methanol-water system yielded 5 constituents (FB1-FB5). The most predominant anti-HIV compd. FB2 (denoted Malachi 4:5-6 or mal.4), which occurs in 0.23% yield, was sepd. from its FB1 isomer (0.13% yield). Compd. FB4 and 2 tricyclic lignans (FB3 and FB5) were also isolated in a substantial amt. for further testing of their anti-HIV activities. These compds. may represent a new class of anti-HIV agents with important clin. relevance.

IT **119584-39-3 174155-42-1 174155-43-2 174155-45-4 174291-51-1 174291-52-2 174291-53-3 174291-54-4 174291-55-5 174291-56-6**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(isolation of anti-HIV-1 lignans from Larrea tridentata by counter-current chromatog.)

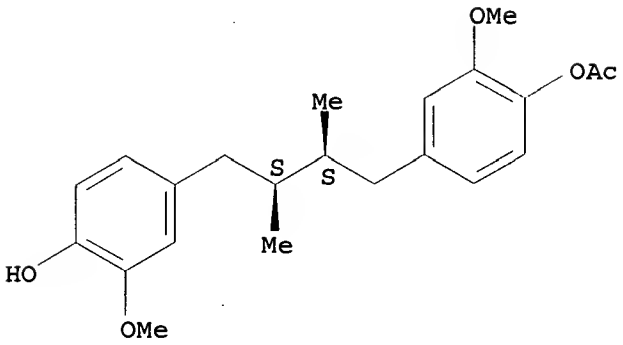
RN 119584-39-3 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



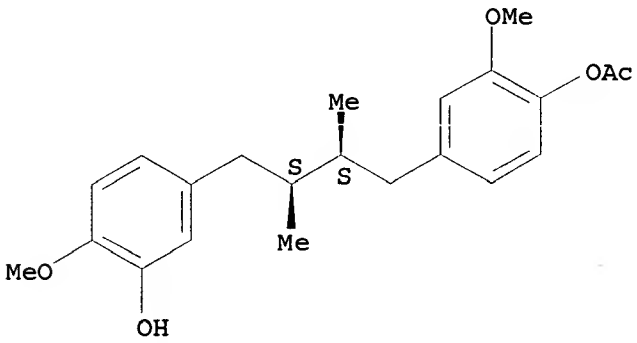
RN 174155-42-1 CAPLUS
CN Phenol, 4-[4-[4-(acetyloxy)-3-methoxyphenyl]-2,3-dimethylbutyl]-2-methoxy-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



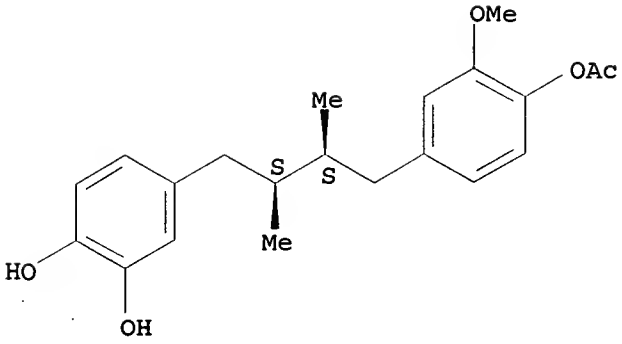
RN 174155-43-2 CAPLUS
CN Phenol, 4-[4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, 1-acetate, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



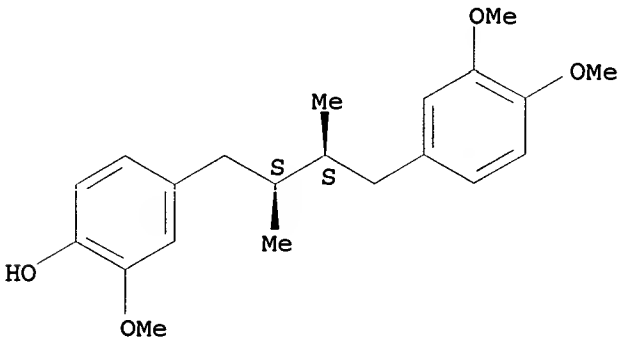
RN 174155-45-4 CAPLUS
CN 1,2-Benzenediol, 4-[4-[4-(acetyloxy)-3-methoxyphenyl]-2,3-dimethylbutyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



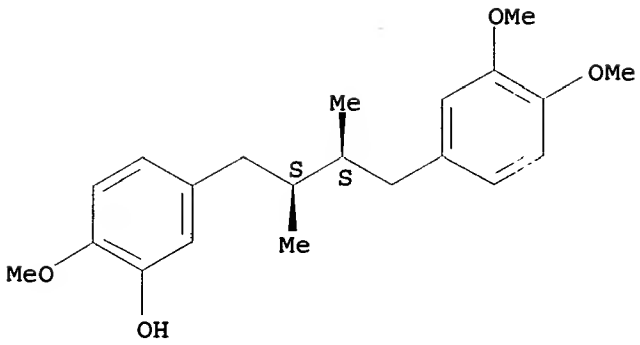
RN 174291-51-1 CAPLUS
CN Phenol, 4-[4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



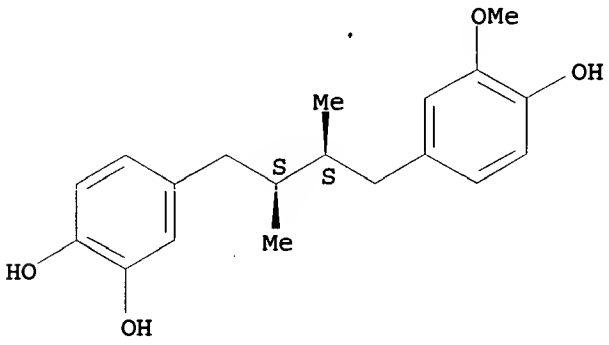
RN 174291-52-2 CAPLUS
CN Phenol, 5-[4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



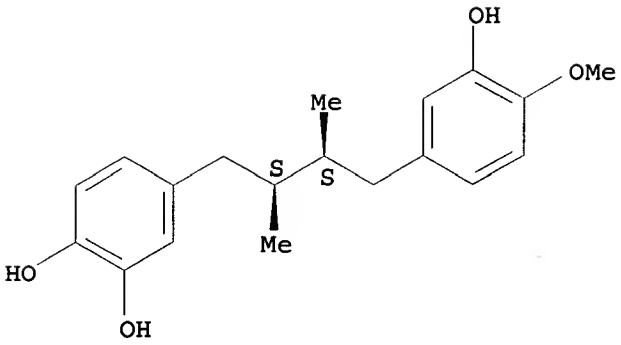
RN 174291-53-3 CAPLUS
CN 1,2-Benzenediol, 4-[4-(4-hydroxy-3-methoxyphenyl)-2,3-dimethylbutyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



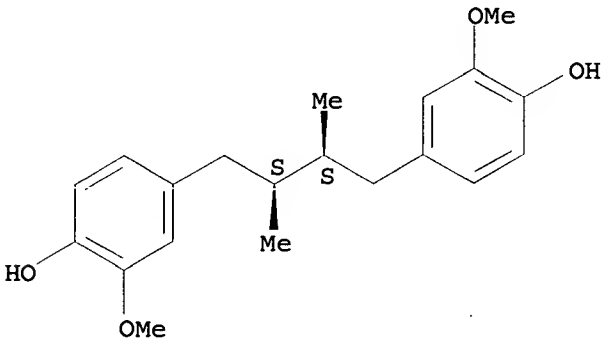
RN 174291-54-4 CAPLUS
CN 1,2-Benzenediol, 4-[4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



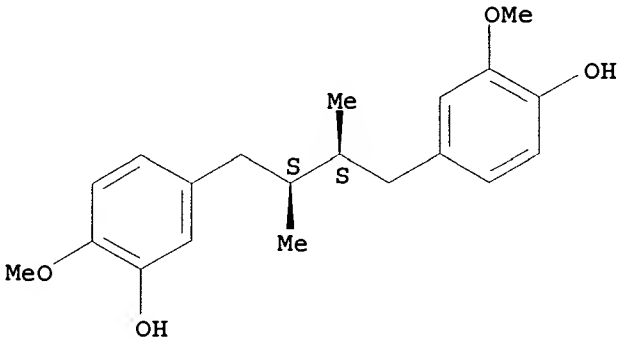
RN 174291-55-5 CAPLUS
CN Phenol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis[2-methoxy-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 174291-56-6 CAPLUS
CN Phenol, 4-[4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



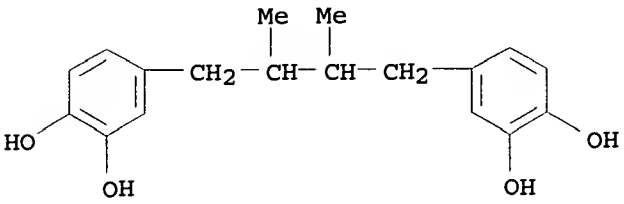
L12 ANSWER 18 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1995:962655 CAPLUS
DOCUMENT NUMBER: 124:105660
TITLE: Inhibition of human immunodeficiency **virus** type 1 transcription and replication by DNA sequence-selective plant lignans
AUTHOR(S): Gnabre, John N.; Brady, John N.; Clanton, David J.; Ito, Yoichiro; Dittmer, Juergen; Bates, Robert B.; Huang, Ru Chih C.
CORPORATE SOURCE: Dep. Biol., Johns Hopkins Univ., Baltimore, MD, 21218, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1995), 92(24), 11239-43
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A plant lignan, 3'-O-Me nordihydroguaiaretic acid (3'-O-Me NDGA, denoted Malachi 4:5-6 or Mal.4; mol. wt. 316), was isolated from Larrea tridentata and found to be able to inhibit human immunodeficiency **virus** (HIV) Tat-regulated transactivation in vivo, induce protection of lymphoblastoid CEM-SS cells from HIV (strain IIIB) killing, and suppress the replication of five HIV-1 strains (WM, MN, VS, JR-CSF, and IIIB) in mitogen-stimulated peripheral blood mononuclear cells, all in a dose-dependent manner. Mal.4 inhibits both basal transcription and Tat-regulated transactivation in vitro. The target of Mal.4 has been localized to nucleotides -87 to -40 of the HIV long terminal repeat. Mal.4 directly and specifically interferes with the binding of Sp1 to Sp1 sites in the HIV long terminal repeat. By inhibiting proviral expression, Mal.4 may be able to interrupt the life cycles of both wild-type and reverse transcriptase or protease mutant **viruses** in HIV-infected patients.

IT **500-38-9**, NDGA **171204-41-4**

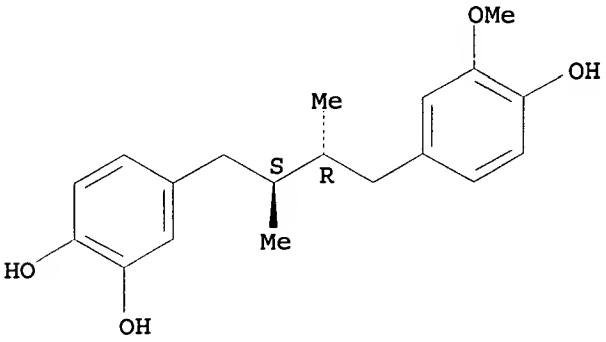
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of human immunodeficiency **virus** type 1 transcription and replication by DNA sequence-selective plant lignans)

RN 500-38-9 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



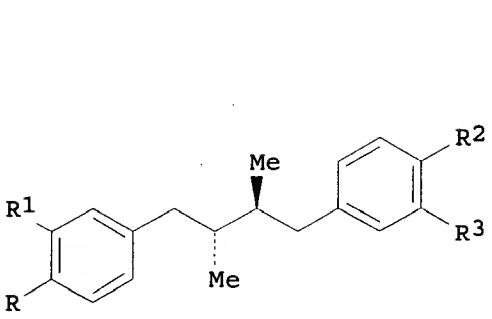
RN 171204-41-4 CAPLUS
CN 1,2-Benzenediol, 4-[4-(4-hydroxy-3-methoxyphenyl)-2,3-dimethylbutyl]-, (R*,S*)-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.

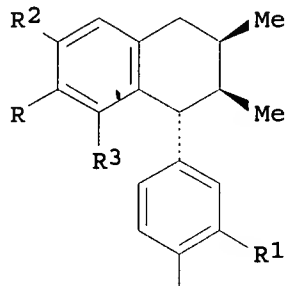


L12 ANSWER 19 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1995:927912 CAPLUS
DOCUMENT NUMBER: 124:25594
TITLE: Characterization of anti-HIV lignans from Larrea tridentata.
AUTHOR(S): Gnabre, John; Huang, Ru Chih C.; Bates, Robert B.; Burns, Jennifer J.; Caldera, Sriyani; Malcomson, Mark E.; McClure, Kelly J.
CORPORATE SOURCE: Dep. Biology, Johns Hopkins Univ., Baltimore, MD, 21218-2685, USA
SOURCE: Tetrahedron (1995), 51(45), 12203-10

CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



II

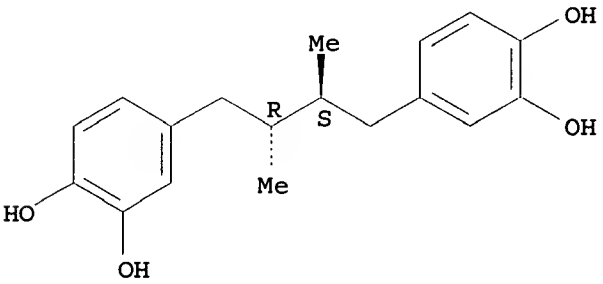
AB Fractions from L. tridentata with anti-HIV-1 activity (specifically, inhibition of HIV Tat transactivation) were analyzed by GC/MS and NMR and found to contain lignans I (R=OH,OMe,OAc;R1,R2=OH,OMe;R3=H,R 1) and II (R=OH,OMe;R1=H,OH,OMe;R2,R3=H,OH). Assay-guided purifn. by countercurrent chromatog. established I (R=R2=R3=OH,R1=OMe) to be esp. active.

IT **27686-84-6P 66322-34-7P 171204-38-9P 171204-39-0P 171204-41-4P 171204-42-5P 171204-43-6P 171439-75-1P 171439-77-3P 171439-78-4P**
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-HIV lignan from Larrea tridentata)

RN 27686-84-6 CAPLUS

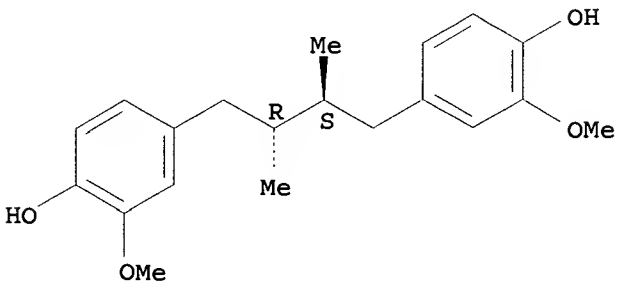
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis-, (R*,S*)-(9CI) (CA INDEX NAME)

Relative stereochemistry.



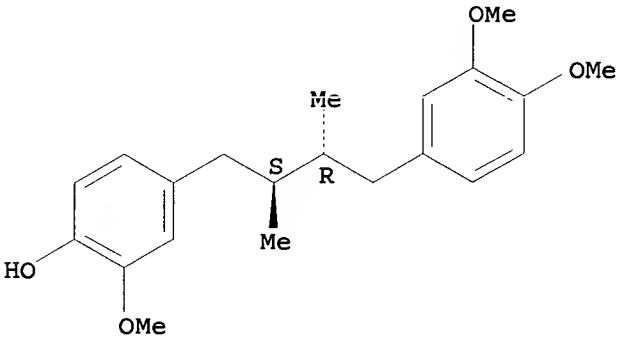
RN 66322-34-7 CAPLUS
CN Phenol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis[2-methoxy-, (R*,S*)-(9CI) (CA INDEX NAME)

Relative stereochemistry.



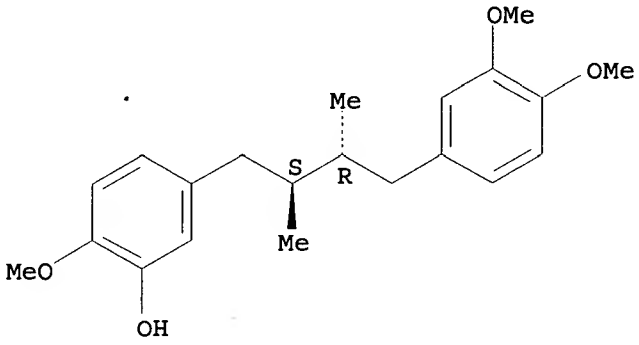
RN 171204-38-9 CAPLUS
CN Phenol, 4-[(2R,3S)-4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



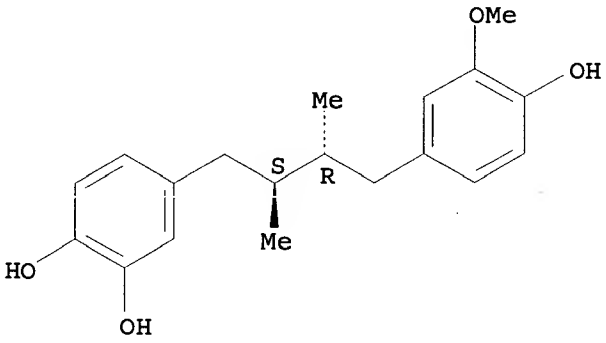
RN 171204-39-0 CAPLUS
CN Phenol, 5-[(2R,3S)-4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



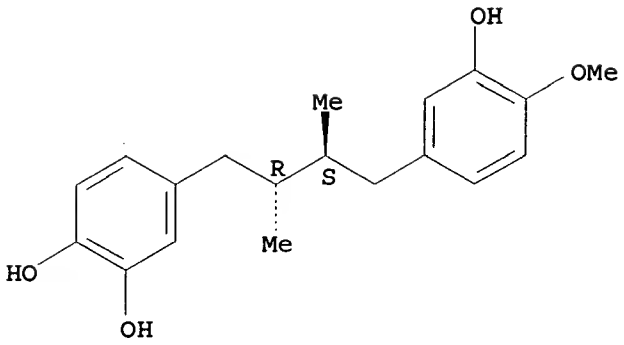
RN 171204-41-4 CAPLUS
CN 1,2-Benzenediol, 4-[4-(4-hydroxy-3-methoxyphenyl)-2,3-dimethylbutyl]-, (R*,S*)-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



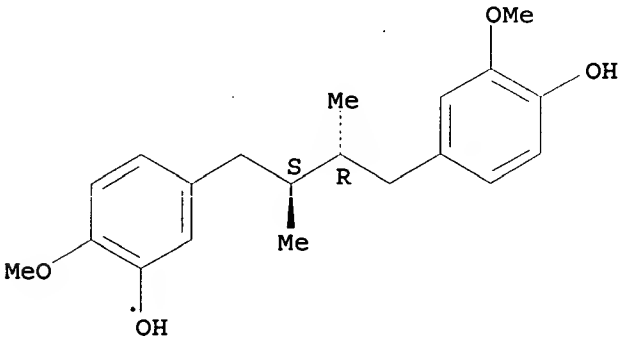
RN 171204-42-5 CAPLUS
CN 1,2-Benzenediol, 4-[4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-, (R*,S*)-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



RN 171204-43-6 CAPLUS
CN Phenol, 4-[(2R,3S)-4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

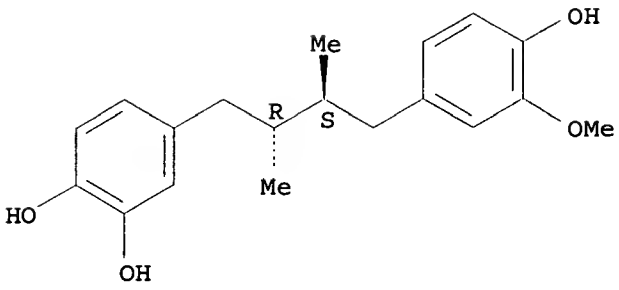


RN 171439-75-1 CAPLUS
CN Phenol, 4-[4-[3(or 4)-(acetyloxy)-4(or 3)-methoxyphenyl]-2,3-dimethylbutyl]-2-methoxy-, (R*,S*)- (9CI) (CA INDEX NAME)

CM 1

CRN 71113-15-0
CMF C19 H24 O4
CDES 2:R*,S*

Relative stereochemistry.



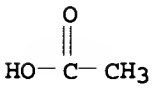
CM 2

CRN 67-56-1
CMF C H4 O

H_3C-OH

CM 3

CRN 64-19-7
CMF C2 H4 O2

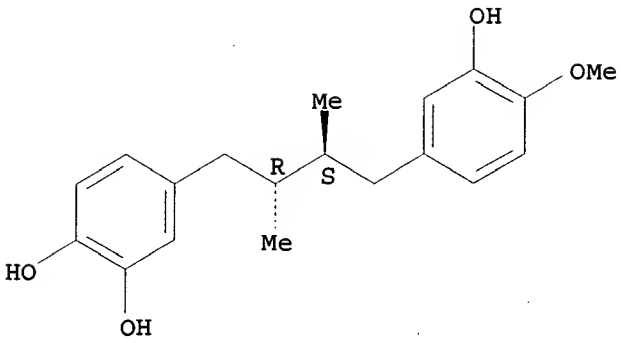


RN 171439-77-3 CAPLUS
CN Phenol, 4(or 5)-[4-(3-hydroxy-4-methoxyphenyl)-2,3-dimethylbutyl]-2-methoxy-, 1-acetate, (R*,S*)- (9CI) (CA INDEX NAME)

CM 1

CRN 171439-76-2
CMF C19 H24 O4
CDES 2:R*,S*

Relative stereochemistry.



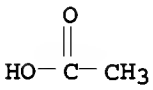
CM 2

CRN 67-56-1
CMF C H4 O

H_3C-OH

CM 3

CRN 64-19-7
CMF C2 H4 O2

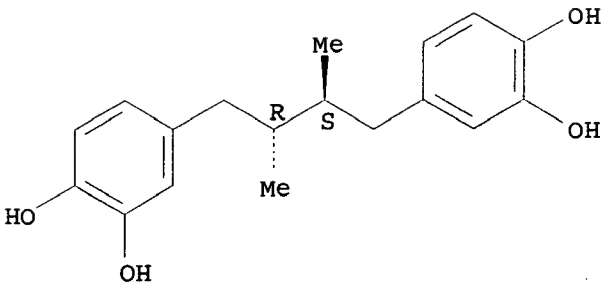


RN 171439-78-4 CAPLUS
CN 1,2-Benzenediol, 4-[4-[3(or 4)-(acetyloxy)-4(or 3)-methoxyphenyl]-2,3-dimethylbutyl]-, (R*,S*)- (9CI) (CA INDEX NAME)

CM 1

CRN 27686-84-6
CMF C18 H22 O4
CDES 2:R*,S*

Relative stereochemistry.



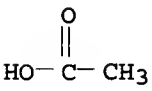
CM 2

CRN 67-56-1
CMF C H4 O

H_3C-OH

CM 3

CRN 64-19-7
CMF C2 H4 O2



L12 ANSWER 20 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1995:464028 CAPLUS
DOCUMENT NUMBER: 122:211984
TITLE: Cell-to-cell contact not soluble factors mediate suppression of lymphocyte proliferation by bovine parainfluenza **virus** type 3
AUTHOR(S): Basaraba, Randall J.; Laegreid, William W.; Brown, Peter R.; Silflow, Ron M.; Brown, Ruth A.; Leid, R. Wes
CORPORATE SOURCE: College of Veterinary Medicine, Kansas State University, Manhattan, KS, 66506-5660, USA
SOURCE: Viral Immunol. (1994), 7(3), 121-32
CODEN: VIIMET; ISSN: 0882-8245
DOCUMENT TYPE: Journal

Searcher : Shears 308-4994

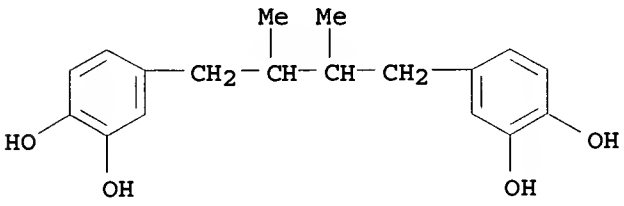
LANGUAGE: English

AB We have previously characterized the ability of parainfluenza **virus** type 3-infected (PIV-3) and noninfected bovine alveolar macrophages (BAM) to support lymphocyte proliferation. While uninfected macrophages support proliferation of lymphocytes stimulated with Con A (Con A), ovalbumin, and interleukin 2 (IL-2), lymphocyte [3H]thymidine incorporation was suppressed in the presence of PIV-3-infected BAM. Since **viral** infection of macrophages has been shown to alter arachidonic acid metab. and cytokine secretion, we have detd. if arachidonate metab. or the lack of IL-1 and IL-2 mediated the suppression of lymphocyte proliferation by PIV-3. Inhibition of arachidonic acid metab. failed to reverse the suppressive effect of **viral** infection as did supplementation of cultures with bovine recombinant IL-1.beta., IL-2, or lymphocyte-conditioned medium. Further, lymphocytes proliferated normally when phys. sepd. from **virus** infected BAM by a semipermeable membrane. Stimulation of lymphocytes in contact with infected BAM resulted in marked suppression of lymphocyte [3H]thymidine incorporation. Interactions between stimulated lymphocytes and PIV-3-infected BAM resulted in PIV-3 infection of lymphocytes. **Virus** infection of lymphocytes was confirmed ultrastructurally by the presence of characteristic parainfluenza **virus** inclusions and **virus** budding from lymphocyte plasma membranes. It was concluded that suppression of lymphocyte proliferation by PIV-3 is mediated in part by infection of stimulated lymphocytes during cell-to-cell contact with BAM.

IT **500-38-9**, Nordihydroguaiaretic acid
RL: BSU (Biological study, unclassified); BIOL (Biological study) (cell-to-cell contact not arachidonic acid metab. inhibitors or cytokines mediate suppression of lymphocyte proliferation by bovine parainfluenza **virus** type 3)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 21 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1995:403097 CAPLUS

DOCUMENT NUMBER: 122:177849

TITLE: E1A-3Y1 cell-specific toxicity of tea polyphenols and their killing mechanism

AUTHOR(S): Mitsui, Takeshi; Yamada, Koji; Yamashita, Kouhei; Matsuo, Noritaka; Okuda, Atsuyuki; Kimura, Genki; Sugano, Michihiro

CORPORATE SOURCE: Faculty Agriculture, Kyushu University, Higashi, 812, Japan

SOURCE: Int. J. Oncol. (1995), 6(2), 377-83
CODEN: IJONES; ISSN: 1019-6439

DOCUMENT TYPE: Journal

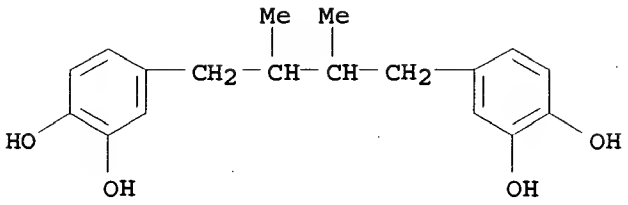
LANGUAGE: English

AB To screen carcinostatic components in foodstuffs, the toxicity of tea polyphenols was compared between rat 3Y1 diploid fibroblasts and a variety of their **virally** transformed cells. Among tea polyphenols tested, epigallocatechin gallate killed 3Y1 cells transformed by E1A gene of human adenovirus type 12 (E1A-3Y1 cells) at a 100 times lower concn. than the parental 3Y1 cells. Epigallocatechin gallate also exerted a strong E1A-3Y1 cell-specific toxicity, while epicatechin and epicatechin gallate did not. When the activity of three antioxidant enzymes was compared between 3Y1 and its transformants, catalase activity was markedly low in the latter, esp. in E1A-3Y1 cells, and the substrate of the enzyme, hydrogen peroxide, exerted a toxicity specific to this cell line. Then the inhibitory activities of various chems. on E1A-3Y1 cell-specific toxicity of phospholipids or catechol were examd. Among lipoxygenase inhibitors, all of the polyphenolic compds. inhibited the toxicity of phospholipids, but not a nonpolyphenolic inhibitor (clofibrate). Two phospholipase A2 inhibitors (dexamethasone and quinacrine) did not inhibit the toxicity. These results indicate that the triphenol structure of the B ring is essential for the E1A-3Y1 cell-specific toxicity of tea polyphenols, and that the decrease in catalase activity is partially responsible for the higher sensitivity of E1A-3Y1 cells against the polyphenols. The inhibitory effect of polyphenolic lipoxygenase inhibitors is ascribed at least in part to their antioxidant activities.

IT **500-38-9**, NDGA
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(effect of lipoxygenase inhibitors and other chems. on cytotoxicity of phosphatidylcholine and catechol)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)

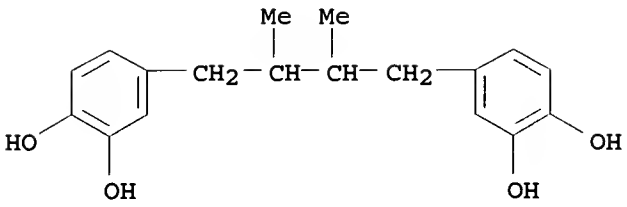


L12 ANSWER 22 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1995:383556 CAPLUS
DOCUMENT NUMBER: 122:150947
TITLE: The non-steroidal anti-inflammatory drug, indomethacin, as an inhibitor of HIV replication
AUTHOR(S): Bourinbaiar, Aldar S.; Lee-Huang, Sylvia
CORPORATE SOURCE: Department of Biochemistry, New York University Medical Center, 550 First Avenue, New York, NY, 10016, USA
SOURCE: FEBS Lett. (1995), 360(1), 85-8
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Indomethacin, a common non-steroidal anti-inflammatory drug (NSAID), has been used to treat rheumatoid arthritis. Although indomethacin has also been used as an immunopotentiator and symptomatic NSAID in AIDS, its effect on HIV replication is unknown. MT-4 lymphocytes were inoculated with HIV in the presence of indomethacin and tested for p24 expression by ELISA. The 50% inhibition (IC50) was 10 .mu.M, corresponding to plasma levels after administration of 50 mg oral indomethacin. The **antiviral** effect appears to be specific since no toxicity has been obsd. at the IC50 dose, and unrelated NSAIDs have not shown the activity at clin. doses. Indomethacin may, thus, represent a new class of anti-HIV drug.

IT **500-38-9**, NDGA
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of NSAIDs on HIV infection)

RN 500-38-9 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 23 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1994:473911 CAPLUS
DOCUMENT NUMBER: 121:73911
TITLE: Inhibitors of arachidonic acid metabolites for preventing neurological damage, and screening method for neuroprotectants
INVENTOR(S): Bernton, Edward W.; Jett, Marti; Gendelman, Howard
PATENT ASSIGNEE(S): United States Department of the Army, USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9412667	A1	19940609	WO 93-US11542	19931129

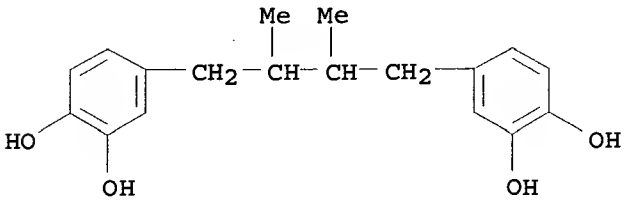
W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.:	US 92-982656	19921127
	US 93-61970	19930902

AB A method is provided for treating encephalitis or encephalopathy secondary to CNS infection by administration of therapeutically effective amts. of compns. which inhibit the release of platelet activation factor and/or arachidonate metabolites. Compns. are disclosed contg. e.g. 11-nor-.DELTA.8-tetrahydrocannabinol-9-carboxylic acid or nordihydroguaiaretic acid. Also provided are methods for screening for compds. that have neuroprotective activity; the methods comprise infecting monocytes or lymphocytes with an infectious organism known to cause neural damage, adding the resulting infected culture to a culture of astrocyte cells, adding a test compd., allowing sufficient time to pass for the prodn. of TNF-alpha, withdrawing aliquots from the supernatant of the culture, adding the aliquots to cultures of neural cells and identifying which supernatants impart a neuroprotective effect.

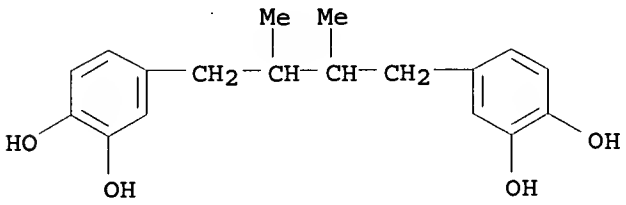
IT **500-38-9**, Nordihydroguaiaretic acid

RL: BIOL (Biological study)
(neuroprotectant compn.contg.)
RN 500-38-9 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 24 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1994:450038 CAPLUS
DOCUMENT NUMBER: 121:50038
TITLE: Antioxidants inhibit stimulation of HIV transcription
AUTHOR(S): Staal, Frank J. T.; Roederer, Mario; Raju, Paul A.; Anderson, Michael T.; Ela, Stephen W.; Herzenberg, Leonard A.; Herzenberg, Leonore A.
CORPORATE SOURCE: Dep. Genet., Stanford Univ. Sch. Med., Stanford, CA, 94305, USA
SOURCE: AIDS Res. Hum. Retroviruses (1993), 9(4), 299-306
CODEN: ARHRE7; ISSN: 0889-2229
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In studies presented here, the authors demonstrate that antioxidants regulate NF.kappa.B activation and signal transduction pathways leading to HIV expression. The authors show (1) that N-acetyl-L-cysteine (NAC), an antioxidant and an efficient glutathione (GSH) precursor, inhibits NF-.kappa.B activation and HIV expression under conditions in which GSH is depleted and NAC cannot be converted to GSH, (2) that the D-stereoisomer of NAC and a wide variety of chem. unrelated antioxidants also inhibit NF-.kappa.B activation and/or transcription directed by the HIV LTR, and (3) that depletion of GSH, the principal intracellular antioxidant, augments HIV prodn. in an acute infection model. Taken together, these findings suggest direct antioxidant action as the mechanism for inhibition of HIV transcription by NAC. They also confirm that GSH, acting in its capacity as an antioxidant, regulates HIV expression and that exogenous antioxidants can potentiate this regulation.
IT **500-38-9**, Nordihydroguaiaretic acid

RL: BIOL (Biological study)
(HIV transcription and replication inhibition by, as antioxidant)
RN 500-38-9 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 25 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1991:115083 CAPLUS
DOCUMENT NUMBER: 114:115083
TITLE: Use of fatty acids or other compounds for the treatment of diseases associated with cytokines, such as alleviation of symptoms of influenza or the common cold
INVENTOR(S): Tan, Yin Hwee; Lim, Louis
PATENT ASSIGNEE(S): National University of Singapore, Singapore
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 396251	A2	19901107	EP 90-303361	19900329
EP 396251	A3	19920708		
R: CH, DE, FR, GB, LI, NL				
JP 03083933	A2	19910409	JP 89-220144	19890825
PRIORITY APPLN. INFO.:			GB 89-7308	19890331
			JP 89-220144	19890825

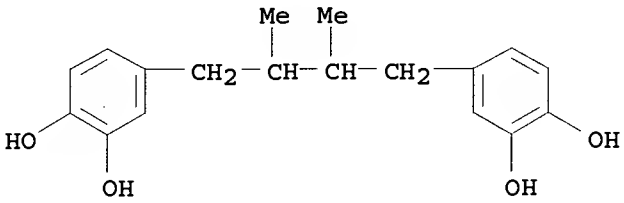
AB Arachidonic acid (I), an arachidonic acid analog, nordihydroguaiaretic acid (II), ketoconazole (III), or quercetin or used in the prepn. of a medicament for use in the treatment of a disease state assocd. with the endogenous presence and/or prodn. of a cytokine. The compds. of the invention can be used to alleviate the symptoms of the common cold or influenza. Thus, 50 .mu.M I, 50 .mu.M II, and 100 .mu.M III inhibited the **antiviral** state induced by .alpha.- or .beta.-interferon by .gtoreq.90%; 50 .mu.M I also inhibited the **antiviral** state induced by

.gamma.-interferon by .gtoreq.80%. Data are presented that suggest that I and other compds. of the invention can diminish the binding of ligands (interferon) to their receptors.

IT **500-38-9**, Nordihydroguaiaretic acid
RL: BIOL (Biological study)
(for cytokine-assocd. disease treatment)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 26 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1991:58721 CAPLUS

DOCUMENT NUMBER: 114:58721

TITLE: Inhibitors of the lipoxygenase pathway specifically block orthopoxvirus replication

AUTHOR(S): Palumbo, G. J.; Buller, R. M. L.

CORPORATE SOURCE: Lab. Viral. Dis., Natl. Inst. Allergy and Infect. Dis., Bethesda, MD, 20892, USA

SOURCE: Virology (1991), 180(1), 457-63
CODEN: VIRLAX; ISSN: 0042-6822

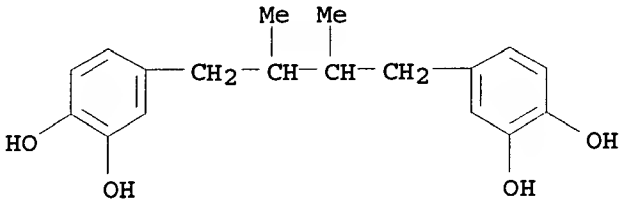
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Inhibitors of arachidonic acid metab., 5,8,11,14-eicosatetraynoic acid (ETYA), BW755c, and nordihydroguaiaretic acid, were found to specifically interfere with the replication of cowpox **virus** (an orthopoxvirus) both in vivo and in vitro. Further studies in vitro showed that the drugs ETYA and BW755c were effective in inhibiting the replication of two addnl. orthopoxviruses, ectromelia and vaccinia **viruses**, but not human parainfluenza **virus**-3. In ETYA-treated and cowpox **virus** -infected cells, early and late gene expression were near normal levels, whereas the assembly of **virus**-specific membranes was severely reduced. These results are compatible with a model of orthopoxvirus replication that has an obligate requirement for arachidonic acid or one of its metabolic forms, possibly in the assembly of **virus**-specific membranes.

IT **500-38-9**, Nordihydroguaiaretic acid
RL: BIOL (Biological study)
(replication of orthopoxvirus inhibition by)

RN 500-38-9 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)

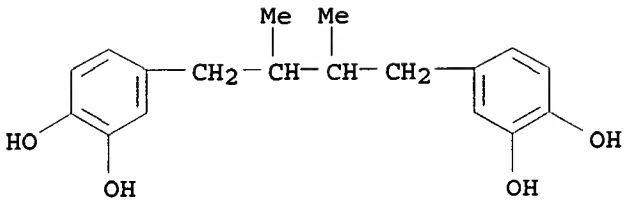


L12 ANSWER 27 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1987:451447 CAPLUS
DOCUMENT NUMBER: 107:51447
TITLE: The effect of modulating the synthesis of arachidonic acid cascade products on HSV lesion recurrence
AUTHOR(S): Yates, F.; Centifanto, Y. M.; Caldwell, D. R.
CORPORATE SOURCE: Sch. Med., Tulane Univ., New Orleans, LA, 70112, USA
SOURCE: Curr. Eye Res. (1987), 6(1), 99-104
CODEN: CEYRDM; ISSN: 0271-3683
DOCUMENT TYPE: Journal
LANGUAGE: English

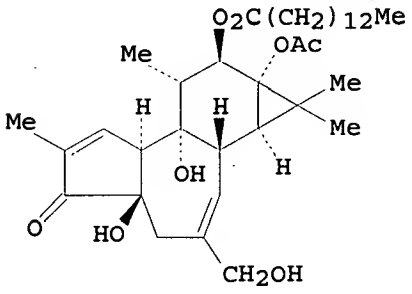
AB Meclofenamate, nordihydroguaiaretic acid (NDGA), and chlorpromazine, which inhibit various products of the arachidonic acid cascade, were compared with saline and corticosteroids in mouse ear models of **herpes** simplex **virus** (**HSV**) recurrence. The relative efficacy in lesion redn. between groups by day 5 post recurrence induction (PRI) is: meclofenamate>steroid = chlorpromazine>NDGA>saline. Meclofenamate, steroid, and chlorpromazine significantly reduced lesions when compared with the saline-treated control mice. NDGA did not significantly reduce lesions by day 5 PRI. Mechanisms of drug action are considered.

IT **500-38-9**, Nordihydroguaiaretic acid
RL: BIOL (Biological study)
(**herpes** simples **virus** lesion recurrence response to, arachidonic metabolite modulation in relation to)

RN 500-38-9 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 28 OF 29 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1986:604506 CAPLUS
DOCUMENT NUMBER: 105:204506
TITLE: Inhibition of 12-O-tetradecanoylphorbol-13 acetate-induced induction of Epstein-Barr **virus** early antigen in Raji cells by some inhibitors of tumor promotion
AUTHOR(S): Saito, Yutaka; Okamoto, Hitoshi; Mizusaki, Shigenobu; Yoshida, Daisuke
CORPORATE SOURCE: Cent. Res. Inst., Japan Tob. Inc., Yokohama, 227, Japan
SOURCE: Cancer Lett. (Shannon, Irel.) (1986), 32(2), 137-44
CODEN: CALEDQ; ISSN: 0304-3835
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

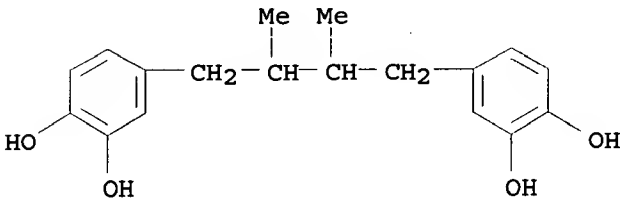
AB The effects of some compds., which have been reported to inhibit tumor promotion in vivo, on the induction of the early antigen (EA) of Epstein-Barr **virus** (EBV) by TPA (I) [16561-29-8] in Raji cells were examd. The inhibitors of the cascade process involving arachidonic acid [506-32-1], indomethacin [53-86-1], nordihydroguaiaretic acid [500-38-9], phenidone [92-43-3] and p-bromophenacyl bromide [99-73-0], effectively inhibited EBV-EA induction by TPA. Two flavonoids, morin

[480-16-0] and kaempferol [520-18-3] also inhibited EA induction. Among antioxidants, butylated hydroxytoluene [128-37-0] effectively inhibited EA induction, though .alpha.-tocopherol [59-02-9] did not show any inhibition of EA induction at concns. of up to 150 .mu.g/mL. N-(6-Aminohexyl)-5-chloro-1-naphthalenesulfonamide [65595-90-6], a calmodulin antagonist, and esculetin [305-01-1] showed inhibitory effects on EA induction, though slight cytotoxicity was obsd. L-1-p-Tosylamino-2-phenylethyl chloromethyl ketone [402-71-1], a protease inhibitor, showed cytotoxicity and no specific inhibition of EA induction. Five kinds of steroids, cortisone [53-06-5], hydrocortisone [50-23-7], prednisolone [50-24-8], dexamethasone [50-02-2] and fluocinolone acetonide [67-73-2] showed no inhibitory effect on EA induction at concns. .ltoreq.100 .mu.g/mL. In addn., the relationship between the inhibition of EBV-EA induction and that of tumor promotion is discussed.

IT **500-38-9**
RL: BIOL (Biological study)
(TPA-induced Epstein-Barr **virus** early antigen in Raji cells response to)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



L12 ANSWER 29 OF 29 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1986:61594 CAPLUS
DOCUMENT NUMBER: 104:61594
TITLE: Reversal of feline retroviral suppression by indomethacin
AUTHOR(S): Lewis, Mark G.; Fertel, Richard H.; Olsen, Richard G.
CORPORATE SOURCE: Dep. Vet. Pathobiol., Ohio State Univ., Columbus, OH, 43210, USA
SOURCE: Leuk. Res. (1985), 9(12), 1451-6
CODEN: LEREDD; ISSN: 0145-2126
DOCUMENT TYPE: Journal
LANGUAGE: English

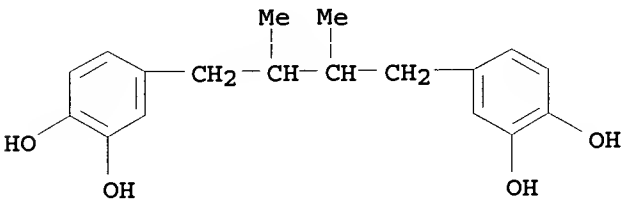
AB The immunosuppressive effect of feline leukemia **virus** (FeLV) and its 15,000-dalton envelope protein (p15E) was studied to

det. if the mechanism of action was due to an increase in prostaglandin prodn. Exogenous PGE1 [745-65-3] and PGE2 [363-24-6] inhibited the normal Con A response of feline peripheral blood lymphocytes (PBL). The addn. of the cyclooxygenase [39391-18-9] inhibitor indomethacin [53-86-1] to cells incubated with FeLV or FeLV p15E and Con A completely abrogated the **viral** suppressive effects. This reversal was titratable and time-dependent. Other nonsteroidal anti-inflammatory inhibitors (NSAI) had similar actions. Indomethacin was also able to increase the suppressed Con A response of PBL from FeLV-infected cats. Upon measurement of PGE2 levels from PBL cultured with FeLV, there was a decrease in PGE2 accumulation assocd. with FeLV presence during the 1st 24 h of culture. These findings indicate that FeLV does not cause its immunosuppressive effects by increasing PG prodn. and suggest that indomethacin and the other tested NSAI do not produce their effect by PG inhibition.

IT **500-38-9**
RL: BIOL (Biological study)
(feline leukemia **virus**-induced immunosuppression inhibition by)

RN 500-38-9 CAPLUS

CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



FILE 'REGISTRY' ENTERED AT 16:52:28 ON 03 JUN 1999

STRUCTURE FILE UPDATES: 28 MAY 99 HIGHEST RN 223764-44-1
DICTIONARY FILE UPDATES: 03 JUN 99 HIGHEST RN 223764-44-1

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=> fil caold; s l13

FILE 'CAOLD' ENTERED AT 16:53:11 ON 03 JUN 1999
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L14 20 L13

=> d 1-20; fil uspat; s l13

L14 ANSWER 1 OF 20 COPYRIGHT 1999 ACS
AN CA65:12772e CAOLD
TI preservation of olive husks with antioxidants and fungistats
AU Savastano, Giulio; Castorina, S.
IT 121-79-9 **500-38-9**

L14 ANSWER 2 OF 20 COPYRIGHT 1999 ACS
AN CA65:9611e CAOLD
TI anal. detn. of 90Sr in foods
AU Davis, Sidney
IT 121-79-9 **500-38-9**

L14 ANSWER 3 OF 20 COPYRIGHT 1999 ACS
AN CA65:7893c CAOLD
TI sepn. and detection of antioxidants in vitamin A oil and vegetable oil by thinlayer chromatography
AU Ishikawa, Seiji; Katsui, G.
IT **500-38-9** 2486-02-4

L14 ANSWER 4 OF 20 COPYRIGHT 1999 ACS
AN CA65:6196c CAOLD
TI changes of lard resulting from the addn. of antioxidants during heating
AU Sedlacek, Bohuslav A. J.
IT 121-79-9 **500-38-9** 1166-52-5

L14 ANSWER 5 OF 20 COPYRIGHT 1999 ACS
AN CA65:4531e CAOLD
TI kinetic method for the detn. of the activity of antioxidants for confectionery production
AU Dremina, N. V.; Li, L.; Gurova-Kuperman, L. A.
IT **500-38-9** 1166-52-5

L14 ANSWER 6 OF 20 COPYRIGHT 1999 ACS
AN CA65:2527h CAOLD
TI complexity of .alpha.-crystallin
AU Bon, Willem F.; Ruttenberg, G. J. C. M.
IT 59-02-9 74-31-7 90-34-6 91-53-2 123-28-4
225-51-4 **500-38-9** 2498-75-1 2896-55-1 4345-03-3
7724-47-2

L14 ANSWER 7 OF 20 COPYRIGHT 1999 ACS
AN CA64:17375g CAOLD
TI oxidn. of phenols - (III) stoichiometries for the oxidn. of some substituted phenols with peroxy radicals
AU Horswill, E. C.; Howard, J. A.; Ingold, K. U.
IT 91-10-1 93-51-6 96-76-4 98-29-3 128-39-2
500-38-9 527-60-6 616-55-7 2219-82-1 2409-55-4

L14 ANSWER 8 OF 20 COPYRIGHT 1999 ACS
AN CA64:17361g CAOLD
TI stability of fat bases applied in galenic prepns. - (III) antioxidants most frequently used in practice and their chem. properties
AU Wisniewski, Wladyslaw; Golucki, Z.
IT 121-79-9 **500-38-9** 1034-01-1 1166-52-5 25013-16-5

L14 ANSWER 9 OF 20 COPYRIGHT 1999 ACS
AN CA64:9890b CAOLD
TI antioxidants for high polymers - (I) inhibiting effects of

antioxidants on autoxidn. of polyethylene, (II) inhibiting effects of antioxidants on autoxidn. of polypropylene
AU Yoshida, Zenichi; Miyoshi
IT 74-31-7 80-05-7 88-58-4 90-66-4 93-46-9
101-87-1 119-47-1 147-47-7 **500-38-9** 2781-09-1
3568-26-1 7005-40-5 7005-43-8 7005-44-9 7005-45-0
7580-46-3

L14 ANSWER 10 OF 20 COPYRIGHT 1999 ACS
AN CA64:5373b CAOLD
TI characteristics of eggplant and avocado polyphenolases
AU Knapp, Frederick W.
IT 103-85-5 148-18-5 331-39-5 **500-38-9**

L14 ANSWER 11 OF 20 COPYRIGHT 1999 ACS
AN CA64:3951a CAOLD
TI bioassay for antioxidants based on protection of Tetrahymena pyriformis from the photodynamic toxicity of benzo(.alpha.)pyrene
AU Epstein, Samuel S.; Saporoschetz, I. B.; Small, M.; Park, W.; Mantel, N.
IT 50-63-5 50-81-7 51-85-4 52-89-1 54-85-3
54-88-6 55-80-1 56-10-0 59-02-9 59-52-9 61-73-4
61-82-5 65-49-6 68-26-8 74-31-7 79-74-3 88-26-6
88-32-4 90-34-6 91-53-2 94-13-3 97-56-3 99-76-3
101-70-2 102-71-6 110-44-1 111-17-1 118-42-3 119-11-9
119-13-1 120-47-8 121-00-6 122-39-4 123-28-4 123-31-9
127-40-2 131-56-6 136-36-7 148-03-8 490-79-9
500-38-9 526-83-0 582-08-1 621-90-9 680-31-9
991-84-4 991-85-5 992-47-2 992-48-3 1421-63-2 1709-70-2
1948-33-0 2058-66-4 2058-67-5 2481-94-9 2512-56-3
2896-55-1 2929-94-4 2985-59-3 3010-57-9 3135-18-0
3147-76-0 3312-50-3 3731-39-3 3732-90-9 4345-03-3
5014-86-8 5302-41-0 5891-06-5 6010-34-0 6029-97-6
6030-03-1 6922-60-7 7050-06-8 16971-82-7 68108-20-3
106979-54-8

L14 ANSWER 12 OF 20 COPYRIGHT 1999 ACS
AN CA64:3282d CAOLD
TI use of polyacrylamide for the purification of diffusion juices of caffeine
AU Filippos'yants, T. T.; Sandomirskaya, G. A.; Pozdnyakova, Z. E.
IT 51-40-1 59-30-3 62-54-4 68-89-3 71-27-2
127-65-1 130-37-0 133-15-3 300-08-3 314-19-2
500-38-9 591-64-0 814-80-2 2944-65-2

L14 ANSWER 13 OF 20 COPYRIGHT 1999 ACS
AN CA63:15050b CAOLD
TI identification of antioxidants in plastics
AU Heide, Ruurd F. van der; Maagdenburg, A. C.; Neut, J. H. van der

IT 96-69-5 111-17-1 121-79-9 123-28-4 500-38-9
693-36-7 1034-01-1 1166-52-5 1335-16-6 1421-63-2 1709-70-2
4066-02-8 28852-17-7

L14 ANSWER 14 OF 20 COPYRIGHT 1999 ACS
AN CA63:13631g CAOLD
TI southern pea lipoxidase
AU Knapp, Frederick W.
IT **500-38-9**

L14 ANSWER 15 OF 20 COPYRIGHT 1999 ACS
AN CA63:10256b CAOLD
TI inhibition of soybean lipoxidase
AU Blain, John A.; Shearer, G.
IT **500-38-9** 1191-85-1 2012-14-8 4102-60-7 4102-62-9
4184-92-3 4184-93-4 4184-96-7

L14 ANSWER 16 OF 20 COPYRIGHT 1999 ACS
AN CA62:16804a CAOLD
TI effect of antioxidants on the liberation of fatty acids from adipose tissues
AU Placer, Zdenek; Petrasek, R.; Veselkova, A.; Rath, R.
IT 99-24-1 144-12-7 **500-38-9** 1034-01-1

L14 ANSWER 17 OF 20 COPYRIGHT 1999 ACS
AN CA55:14753b CAOLD
TI feed supplement for hens
AU Koffler, Maximilian
DT Patent
IT **66322-34-7** **112867-79-5**

L14 ANSWER 18 OF 20 COPYRIGHT 1999 ACS
AN CA55:4468e CAOLD
TI intermediates necessary in the synthesis of resinols and derivs. - (V), (VI)
AU Traverso, Giorgio
IT 721-42-6 833-67-0 1835-02-5 4650-69-5 4650-71-9
4687-37-0 5701-82-6 51487-58-2 53293-07-5 **66322-34-7**
101499-83-6 102454-96-6 102655-73-2 102761-86-4 102890-88-0
103042-42-8 103239-13-0 111612-07-8 **112867-79-5**
115322-45-7 115386-03-3 124117-73-3

L14 ANSWER 19 OF 20 COPYRIGHT 1999 ACS
AN CA51:17851i CAOLD
TI meso-dihydroguaiaretic acid and its derivs.
AU Schrecker, Anthony W.
IT 500-40-3 5507-27-7 5701-82-6 7461-04-3 24289-99-4
42923-56-8 63339-53-7 **66322-34-7** 93578-43-9 93578-48-4
93609-04-2 95810-13-2 102757-68-6 102758-58-7 103402-11-5

112867-79-5 121271-89-4 124117-73-3

L14 ANSWER 20 OF 20 COPYRIGHT 1999 ACS
AN CA51:4330f CAOLD
TI abs. configuration of dihydroguaiaretic acid
AU Carnmalm, Bernt
IT 5701-82-6 7475-92-5 13545-04-5 26979-55-5 58372-16-0
66322-34-7 92203-55-9 100523-76-0 101257-25-4 102471-96-5
112867-79-5

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(FILE 'USPATFULL' ENTERED AT 16:53:20 ON 03 JUN 1999)
L15 43 SEA ABB=ON PLU=ON L13
L16 13 SEA ABB=ON PLU=ON L15 AND (ANTIVIR? OR VIRUS? OR VIRAL? OR (HSV OR HV)(S)HERPES? OR HERPES?)

L16 ANSWER 1 OF 13 USPATFULL
ACCESSION NUMBER: 1998:143662 USPATFULL
TITLE: Nontoxic extract of Larrea tridentata and method of making same
INVENTOR(S): Sinnott, Robert A., Chandler, AZ, United States
Clark, W. Dennis, Phoenix, AZ, United States
DeBoer, Kenneth Frank, Belgrade, MT, United States
PATENT ASSIGNEE(S): Larreacorp, Ltd., Chandler, AZ, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5837252	19981117
APPLICATION INFO.:	US 96-726686	19961007 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Witz, Jean C.
ASSISTANT EXAMINER: Hanley, Susan
LEGAL REPRESENTATIVE: Benson, David K.; Nichols, Steven L.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 692
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A nontoxic, therapeutic agent having pharmacological activity comprising concentrated extract of Larrea tridentata plant material and ascorbic acid, an ascorbic acid ester, an ascorbic acid salt, butylated hydroxyanisole, butylated hydroxytoluene, hydrogen sulfide, hypophosphorous acid, monothioglycerol, potassium bisulfite, propyl gallate, sodium bisulfite, sodium hydrosulfite, sodium thiosulfate, sulfur dioxide, sulfurous acid, a tocopherol, or vitamin E is made by a process in which the plant

material is extracted using an organic solvent, preferably acetone, and is then saturated with one of the listed reducing agents acid to reduce the toxic NDGA quinone, which naturally occurs in the plant material, to NDGA itself. Additional amounts of ascorbic acid, an ascorbic acid ester, an ascorbic acid salt, butylated hydroxyanisole, butylated hydroxytoluene, hydrogen sulfide, hypophosphorous acid, monothioglycerol, potassium bisulfite, propyl gallate, sodium bisulfite, sodium hydrosulfite, sodium thiosulfate, sulfur dioxide, sulfurous acid, a tocopherol, or vitamn E may be added to the extract to inhibit the natural oxidation of the NDGA into the toxic NDGA quinone in vivo, or during processing or storage. The resulting extract is useful in the treatment of **viral** diseases caused by **viruses** from the **Herpesviridae** family or **viruses** which require the Sp1 class of proteins to initiate **viral** replications. The resulting compound can also be used as an anti-inflammatory when the inflaatory diseases are mediated by the effects of leukotrienes. The listed reducing agents can also be used to stabilize NDGA as a therapeutic agent or a food additive.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 2 OF 13 USPATFULL

ACCESSION NUMBER: 97:122847 USPATFULL

TITLE: Treatment for biological damage using a colony stimulating factor and a biological modifier

INVENTOR(S): Zimmerman, Robert, Lafayette, CA, United States
Marafino, Jr., Benedict J., San Francisco, CA, United States

PATENT ASSIGNEE(S): Chiron Corporation, Emeryville, CA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5702697	19971230
APPLICATION INFO.:	US 95-457629	19950601 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 94-289844, filed on 12 Aug 1994, now patented, Pat. No. US 5508031 which is a continuation of Ser. No. US 93-49070, filed on 16 Apr 1993, now abandoned which is a continuation of Ser. No. US 90-626975, filed on 12 Dec 1990, now abandoned which is a division of Ser. No. US 89-399386, filed on 25 Aug 1989, now patented, Pat. No. US 4985241 which is a continuation of Ser. No. US 87-113643, filed on 26 Oct 1987, now abandoned which is a continuation-in-part of Ser. No. US 86-933475, filed on 21 Nov 1986, now abandoned

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Ulm, John
ASSISTANT EXAMINER: Mertz, Prema
LEGAL REPRESENTATIVE: Gass, David A.; Savereide, Paul B.; Blackburn, Robert P.
NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM: 1
LINE COUNT: 1705
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Damage to cells, tissue and other body parts in a mammalian host may be treated by using a colony stimulating factor in conjunction with at least one biological modifier, which may be a free radical scavenger or a metabolic inhibitor. The biological modifier is preferably uric acid, buthionine sulphoximine, vitamin C, aspirin, or nordihydroguaiaretic acid. Such a combination may be used to treat, for example, cancer, infectious diseases, and damage caused by radiation therapy, high oxygen tension, and chemotherapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 3 OF 13 USPATFULL
ACCESSION NUMBER: 97:122844 USPATFULL
TITLE: Compositions for treating corns, calluses and warts
INVENTOR(S): Chamness, Thomas W., Memphis, TN, United States
PATENT ASSIGNEE(S): Schering-Plough HealthCare Products, Inc., United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5702694	19971230	
	WO 9505156	19950223	
APPLICATION INFO.:	US 96-596219	19960212	(8)
	WO 94-US8315	19940811	
		19960212	PCT 371 date
		19960212	PCT 102(e) date

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 93-107553, filed on 17 Aug 1993
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Shelborne, Kathryne E.
LEGAL REPRESENTATIVE: Boxer, Matthew; Maitner, John
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 934
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Topical compositions for the treatment of corns, calluses and warts comprising a benzenediol or a substituted 1,2-benzenediol and a pharmaceutically acceptable carrier, are described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 4 OF 13 USPATFULL

ACCESSION NUMBER:	97:83609 USPATFULL
TITLE:	Treatment for biological damage using tumor necrosis factor and a free-radical scavenger
INVENTOR(S):	Zimmerman, Robert, Lafayette, CA, United States Marafino, Jr., Benedict J., San Francisco, CA, United States
PATENT ASSIGNEE(S):	Chiron Corporation, Emeryville, CA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5667776	19970916
APPLICATION INFO.:	US 95-456947	19950601 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 94-289844, filed on 12 Aug 1994, now patented, Pat. No. US 5508031 which is a continuation of Ser. No. US 93-49070, filed on 16 Apr 1993, now abandoned which is a continuation of Ser. No. US 90-626975, filed on 12 Dec 1990, now abandoned which is a division of Ser. No. US 89-399386, filed on 25 Aug 1989, now patented, Pat. No. US 4985241 which is a continuation of Ser. No. US 87-113643, filed on 26 Oct 1987, now abandoned which is a continuation-in-part of Ser. No. US 86-933475, filed on 21 Nov 1986, now abandoned

DOCUMENT TYPE:	Utility
PRIMARY EXAMINER:	Ulm, John
ASSISTANT EXAMINER:	Mertz, Prema
LEGAL REPRESENTATIVE:	Gass, David A.; Savereide, Paul B.; Blackburn, Robert P.
NUMBER OF CLAIMS:	30
EXEMPLARY CLAIM:	1
LINE COUNT:	1648

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Damage to cells, tissue and other body parts in a mammalian host may be treated by using a tumor necrosis factor in conjunction with at least one biological modifier, which may be a free radical scavenger or a metabolic inhibitor. The biological modifier is preferably uric acid, buthionine sulphoximine, vitamin C, aspirin, or nordihydroguaiaretic acid. Such a combination may be used to treat, for example, cancer, infectious diseases, and damage caused by radiation therapy, high oxygen tension, and chemotherapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 5 OF 13 USPATFULL
ACCESSION NUMBER: 97:78478 USPATFULL
TITLE: Compounds for the suppression of HIV Tat transactivation
INVENTOR(S): Huang, Ru Chih C., Baltimore, MD, United States
Gnabre, John N., Baltimore, MD, United States
PATENT ASSIGNEE(S): The Johns Hopkins University, Baltimore, MD, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5663209	19970902
APPLICATION INFO.:	US 96-627588	19960404 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 94-316341, filed on 30 Sep 1994
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Rollins, John W.
LEGAL REPRESENTATIVE: Cushman Darby & Cushman IP Group Pillsbury Madison & Sutro LLP
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Figure(s); 7 Drawing Page(s)
LINE COUNT: 765
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention reveals the isolation, purification and characterization from the creosote bush Larrea tridentata of compounds of the structural formula: ##STR1## where R.sub.1, R.sub.2, R.sub.3 and R.sub.4 are each selected from the group consisting of HO--, CH.sub.3 O-- and CH.sub.3 (C.dbd.O)O--, provided that R.sub.1, R.sub.2, R.sub.3 and R.sub.4 are not each HO-- simultaneously. Each compound is a derivative of 1,4-bis-(3,4-dihydroxyphenyl)-2,3-dimethylbutane (nordihydroquaiaretic acid, NDGA). In addition, NDGA and each derivative can be used in a method to suppress Tat transactivation of a lentivirus, including the HIV **virus**, in a cell by administering NDGA or a derivative of NDGA to the cell.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 6 OF 13 USPATFULL
ACCESSION NUMBER: 96:68050 USPATFULL
TITLE: Treatment of multidrug resistant diseases
INVENTOR(S): Howell, Stephen, Del Mar, CA, United States
Khandwala, Atul, Edgewater, NJ, United States
Sachdey, Om P., New City, NY, United States
Smith, Charles G., Rancho Santa Fe, CA, United States
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., Tarrytown, NY, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5541232	19960730
APPLICATION INFO.:	US 94-264740	19940623 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 93-81663, filed on 23 Jun 1993, now patented, Pat. No. US 5409690
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Criares, Theodore J.
LEGAL REPRESENTATIVE: Weiser & Associates
NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 964
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method and composition for treating multidrug resistance in a mammal, in which the composition includes NDGA or an analog of NDGA in accordance with the following formula: ##STR1## wherein R.sub.1 and R.sub.2 are independently H, lower alkyl or lower acyl;

R.sub.3, R.sub.4, R.sub.5, and R.sub.6 are independently H or lower alkyl;

R.sub.7, R.sub.8 and R.sub.9 are independently H, hydroxy, lower alkoxy or lower acyloxy; and

R.sub.10, R.sub.11, R.sub.12 and R.sub.13 are independently H or lower alkyl, in a pharmaceutically acceptable vehicle.

The method is particularly suitable for administering an antineoplastic agent, and the composition includes the combination of NDGA, or an analog with such an antineoplastic agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 7 OF 13 USPATFULL
ACCESSION NUMBER: 96:31583 USPATFULL
TITLE: Method for treating biological damage using a free-radial scavenger and interleukin-2
INVENTOR(S): Zimmerman, Robert, Lafayette, CA, United States
Marafino, Jr., Benedict J., San Francisco, CA, United States
PATENT ASSIGNEE(S): Cetus Oncology Corporation, Emeryville, CA, United States (U.S. corporation)

	NUMBER	DATE

PATENT INFORMATION: US 5508031 19960416
APPLICATION INFO.: US 94-289844 19940812 (8)
RELATED APPLN. INFO.: Continuation of Ser. No. US 93-49070, filed on 16 Apr 1993, now abandoned which is a continuation of Ser. No. US 90-626975, filed on 12 Dec 1990, now abandoned which is a division of Ser. No. US 89-399386, filed on 25 Aug 1989, now patented, Pat. No. US 4985241 which is a continuation of Ser. No. US 87-113643, filed on 26 Oct 1987, now abandoned which is a continuation-in-part of Ser. No. US 86-933475, filed on 21 Nov 1986, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Walsh, Stephen G.
LEGAL REPRESENTATIVE: Gass, David A.; Savereide, Paul B.; Blackburn, Robert P.
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
LINE COUNT: 1581
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Damage to cells, tissue and other body parts in a mammalian host may be treated by using a lymphokine or cytotoxin in conjunction with at least one biological modifier, which may be a free radical scavenger or a metabolic inhibitor. The biological modifier is preferably uric acid, buthionine sulphoximine, vitamin C, aspirin, or nordihydroguaiaretic acid. Such a combination may be used to treat, for example, cancer, infectious diseases, and damage caused by radiation therapy, high oxygen tension, and chemotherapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 8 OF 13 USPATFULL
ACCESSION NUMBER: 94:1453 USPATFULL
TITLE: Methods of treating tumors with compositions of catecholic butanes
INVENTOR(S): Neiss, Edward S., Denver, CO, United States
Allen, Larry M., Golden, CO, United States
Jordan, Russell T., Fort Collins, CO, United States
PATENT ASSIGNEE(S): Block/Chemex, G.P., Jersey City, NJ, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5276060	19940104
APPLICATION INFO.:	US 91-685609	19910415 (7)

RELATED APPLN. INFO.: Division of Ser. No. US 87-57481, filed on 3 Jun 1987, now patented, Pat. No. US 5008294 which is a continuation-in-part of Ser. No. US 87-52420,

filed on 4 May 1987, now abandoned which is a continuation of Ser. No. US 85-699923, filed on 11 Feb 1985, now abandoned which is a continuation-in-part of Ser. No. US 84-578501, filed on 9 Apr 1984, now abandoned which is a continuation-in-part of Ser. No. US 83-465631, filed on 10 Feb 1983, now abandoned which is a continuation-in-part of Ser. No. US 82-365781, filed on 5 Apr 1982, now abandoned which is a continuation-in-part of Ser. No. US 79-49886, filed on 19 Jun 1979, now abandoned

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Rollins, John W.
LEGAL REPRESENTATIVE: Kenyon & Kenyon
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
LINE COUNT: 825
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to methods useful in the treatment of benign, premalignant and malignant solid tumors, especially those of the skin comprising methods for the administration of pharmacologically active compositions containing catecholic butanes. The invention also relates to methods of preventing the occurrence of tumors, and the use of catecholic butanes as a sunscreening agent. The preferred catecholic butane is nordihydroguaiaretic acid. The preferred methods of application of the compositions containing catecholic butanes are by topical application and intratumor injection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 9 OF 13 USPATFULL
ACCESSION NUMBER: 91:30516 USPATFULL
TITLE: Methods of treating tumors with compositions of catecholic butanes
INVENTOR(S): Neiss, Edward S., Denver, CO, United States
Allen, Larry M., Golden, CO, United States
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., Denver, CO, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5008294	19910416
APPLICATION INFO.:	US 87-57481	19870603 (7)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 87-52120, filed on 4 May 1987, now abandoned which is a continuation of Ser. No. US 85-699923, filed on 11 Feb 1985, now abandoned which is a continuation-in-part of Ser. No. US 84-578501,

filed on 9 Apr 1984, now abandoned which is a continuation-in-part of Ser. No. US 83-465631, filed on 10 Feb 1983, now abandoned which is a continuation-in-part of Ser. No. US 82-365781, filed on 5 Apr 1982, now abandoned which is a continuation-in-part of Ser. No. US 79-49886, filed on 19 Jun 1979, now abandoned

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Rollins, John W.
LEGAL REPRESENTATIVE: Kenyon & Kenyon
NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
LINE COUNT: 983
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to methods useful in the treatment of benign, premalignant and malignant solid tumors, especially those of the skin comprising methods for the administration of pharmacologically active compositions containing catecholic butanes. The invention also relates to methods of preventing the occurence of tumors, and the use of catecholic butanes as a sunscreening agent. The preferred catecholic butane is nordihydroguaiaretic acid. The preferred methods of application of the compositions containing catecholic butanes are by topical application and intratumor injection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 10 OF 13 USPATFULL
ACCESSION NUMBER: 91:4937 USPATFULL
TITLE: Therapeutic combination of free-radical scavenger and tumor necrosis factor
INVENTOR(S): Zimmerman, Robert, Lafayette, CA, United States
Marafino, Jr., Benedict J., San Francisco, CA, United States
PATENT ASSIGNEE(S): Cetus Corporation, Emeryville, CA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 4985241	19910115
APPLICATION INFO.:	US 89-399386	19890825 (7)

RELATED APPLN. INFO.: Continuation of Ser. No. US 87-113643, filed on 26 Oct 1987, now abandoned which is a continuation-in-part of Ser. No. US 86-933475, filed on 21 Nov 1986, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Draper, Garnette D.
LEGAL REPRESENTATIVE: Giotta, Gregory J.; Hasak, Janet E.; Halluin, Albert P.
Searcher : Shears 308-4994

NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
LINE COUNT: 1333
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Damage to cells, tissue and other body parts in a mammalian host may be treated by using a lymphokine or cytotoxin in conjunction with at least one biological modifier, which may be a free radical scavenger or a metabolic inhibitor. The lymphokine or cytotoxin is preferably tumor necrosis factor and the biological modifier is preferably uric acid, buthionine sulphoximine, vitamin C, aspirin, or nordihydroguaiaretic acid. Such a combination may be used to treat, for example, cancer, infectious diseases, and damage caused by radiation therapy, high oxygen tension, and chemotherapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 11 OF 13 USPATFULL
ACCESSION NUMBER: 90:5872 USPATFULL
TITLE: Pharmaceutical vehicles for exhancing penetration and retention in the skin
INVENTOR(S): Allen, Larry M., Denver, CO, United States
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., Denver, CO, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 4895727	19900123	
APPLICATION INFO.:	US 85-730682	19850503	(6)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Maple, John S.
LEGAL REPRESENTATIVE: Kenyon & Kenyon
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 1116
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention is a method of inducing a reservoir effect in skin and mucous membranes so as to enhance penetration and retention and reduce transdermal flux of topically applied therapeutic and cosmetic pharmacologically active agents. The invention also relates to topical treatment methods involving such reservior effect enhancers, and to pharmaceutical compositions containing them.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 12 OF 13 USPATFULL
ACCESSION NUMBER: 89:92343 USPATFULL
TITLE: Compositions of catecholic butanes with zinc

INVENTOR(S): Jordan, Russell T., Fort Collins, CO, United States
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., Denver, CO, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 4880637	19891114
APPLICATION INFO.:	US 86-924620	19861028 (6)

DISCLAIMER DATE: 20050927
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 85-699923, filed on 11 Feb 1985, now abandoned which is a continuation-in-part of Ser. No. US 84-578501, filed on 9 Apr 1984, now abandoned which is a continuation-in-part of Ser. No. US 83-465631, filed on 10 Feb 1983, now abandoned which is a continuation-in-part of Ser. No. US 82-365781, filed on 5 Apr 1982, now abandoned which is a continuation-in-part of Ser. No. US 79-49886, filed on 19 Jun 1979, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Rollins, John W.
LEGAL REPRESENTATIVE: Kenyon & Kenyon
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
LINE COUNT: 1185
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides new compositions comprising catecholic butanes and ionic zinc. The invention also relates to pharmacologically active compositions comprising said new compositions, which are useful in the treatment of benign, premalignant and malignant solid tumors, especially those of the skin. The ionic zinc may be in the form of a zinc salt, and the preferred catecholic butane is nordihydroguaiaretic acid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 13 OF 13 USPATFULL
ACCESSION NUMBER: 88:62483 USPATFULL
TITLE: Modification of plant extracts from zygophyllaceae and pharmaceutical use therefor
INVENTOR(S): Jordan, Russell T., Fort Collins, CO, United States
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., Denver, CO, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 4774229	19880927

APPLICATION INFO.: US 86-860654 19860507 (6)
RELATED APPLN. INFO.: Continuation of Ser. No. US 82-365784, filed on 5 Apr 1982, now abandoned which is a continuation-in-part of Ser. No. US 79-49886, filed on 19 Jun 1979, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Rollins, John
LEGAL REPRESENTATIVE: Kenyon & Kenyon
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
LINE COUNT: 835
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A mixture of an extract from a plant belonging to the Zygophyllaceae family containing phenolic compositions and a nonalkali metal salt is useful as a pharmaceutical agent, for example, in the treatment of cancer, nonmalignant tumors, osteomyelitis, psoriasis and warts.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 5898023 27 APR 1999
DE 19849755 29 APR 1999
EP 913456 06 MAY 1999
JP 11116551 27 APR 1999
WO 9922383 06 MAY 1999

MARPAT structure search limits have been raised.
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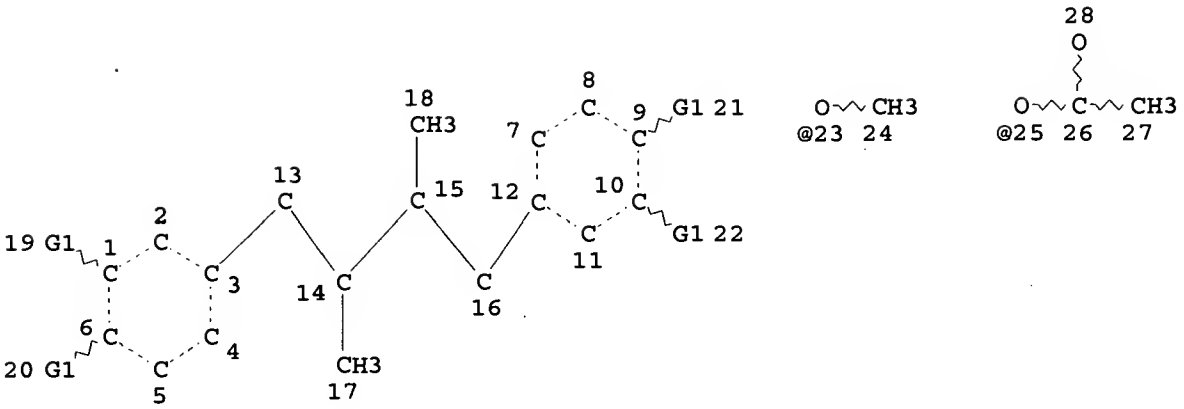
L5 STR



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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L18 17 SEA FILE=MARPAT SSS FUL L5 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 9546 ITERATIONS (1 INCOMPLETE) 17 ANSWERS
SEARCH TIME: 00.01.03

=> d 1-17 .bevmar; fil marpatprev

L18 ANSWER 1 OF 17 MARPAT COPYRIGHT 1999 ACS
(ALL HITs ARE ITERATION INCOMPLETES)
ACCESSION NUMBER: 130:242298 MARPAT
TITLE: Preparation of phthalaldehyde derivatives as antidiabetics
INVENTOR(S): Vertesy, Laszlo; Kurz, Michael; Schindler, Peter; Stump, Heike
PATENT ASSIGNEE(S): Hoechst Marion Roussel Deutschland GmbH, Germany
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 902002	A1	19990317	EP 98-116936	19980908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19740080	A1	19990318	DE 97-19740080	19970912
CA 2246928	AA	19990312	CA 98-2246928	19980911
PRIORITY APPLN. INFO.:			DE 97-19740080	19970912

AB Phthalaldehyde derivs., esp. Hericenal C are useful for the treatment of metabolic disorders, esp. glucose metabolic disorders and for the treatment of Diabetes mellitus. Hericenal A, B and C were purified by column chromatog. of cell culture solns. from Hericium erinaceus. The effectiveness of the compds. in the inhibition of glucose 6-phosphate translocase was demonstrated for Hericenal, A, B, and C at 8, 8.6, and 8.6 .mu.g/mL.

IC ICM C07C047-544
ICS C07C047-56; A61K031-11

CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 1, 26

ST phthalaldehyde deriv antidiabetic; hericenal glucose phosphate translocase inhibition antidiabetic

IT New natural products
(Hericenal A (benzenoid))

IT New natural products
(Hericenal B (benzenoid))

IT New natural products
(Hericenal C (benzenoid))

IT Glucose transporters
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(glucose phosphate-transporting; prepn. of phthalaldehyde derivs. as antidiabetics)

IT Molecular structure (natural product)
(of Hericenal A (benzenoid))

IT Molecular structure (natural product)
(of Hericenal B (benzenoid))

IT Molecular structure (natural product)
(of Hericenal C (benzenoid))

IT Antidiabetic agents
Carbohydrate metabolic diseases
Hericium erinaceus
(prepn. of phthalaldehyde derivs. as antidiabetics)

IT 50-99-7, Glucose, biological studies
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU

(Occurrence); PROC (Process)
(metabolic disorders; prepn. of phthalaldehyde derivs. as antidiabetics)

IT 483-53-4, Flavipin 643-79-8D, Phthalaldehyde, derivs. 221322-84-5, Hericenal A 221322-87-8, Hericenal B 221322-90-3, Hericenal C
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(prepn. of phthalaldehyde derivs. as antidiabetics)

L18 ANSWER 2 OF 17 MARPAT COPYRIGHT 1999 ACS
ACCESSION NUMBER: 128:290238 MARPAT
TITLE: Use of bisphenolic compounds to treat type II diabetes
INVENTOR(S): Khandwala, Atul S.; Luo, Jian
PATENT ASSIGNEE(S): Shaman Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9815266	A1	19980416	WO 97-US18109	19971006
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, ID, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5827898	A	19981027	US 96-726591	19961007
AU 9850795	A1	19980505	AU 98-50795	19971006
PRIORITY APPLN. INFO.:			US 96-726591	19961007
			WO 97-US18109	19971006

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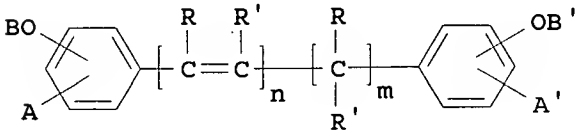


I

AB Methods are provided for treatment of non-insulin-dependent diabetes

mellitus, for reducing blood glucose levels, or hyperglycemia. The methods entail administering to a mammal in need of such treatment a therapeutically effective amt. of a compn. whose active ingredient consists essentially of a compd. I [R, R' = H, (un)substituted C1-C20 alkyl, (un)substituted C2-C20 alkenyl, or R and R' together form cycloalk(en)yl ring; (C(R):C(R')), (C(R)(R')) are the same or different; A, A' = C2-C20 acylamino, C2-C20 acyloxy, C2-C20 alcanoyl, etc.; B, B' = H, C2-C20 alkanoyl, C3-C20 alkenoyl, C2-C20 alkenyl, etc.; n, m = 0-6] or a pharmaceutically acceptable salt thereof. Also provided are methods of treatment using a bisphenolic compd. in conjunction with another hypoglycemic or hypolipidemic agent. The hypoglycemic activity of nordihydroguaiaretic acid is described.

IC ICM A61K031-05

CC 1-10 (Pharmacology)

ST bisphenolic compd antidiabetic hypoglycemic; nordihydroguaiaretic acid hypoglycemic

IT Antidiabetic agents
Glucose transport
Hypolipemic agents
(bisphenolic compds. to treat type II diabetes, and combinations with other agents)

IT Sulfonylureas
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bisphenolic compds. to treat type II diabetes, and combinations with other agents)

IT .beta.-Adrenoceptor antagonists
(.beta.3-adrenoceptor antagonists; bisphenolic compds. to treat type II diabetes, and combinations with other agents)

IT 56-03-1D, Biguanide, derivs. 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 500-38-9, Nordihydroguaiaretic acid 504-78-9D, Thiazolidine, derivs. 657-24-9, Metformin 692-13-7, Buformin 968-81-0, Acetohexamide 1156-19-0, Tolazamide 9004-10-8, Insulin, biological studies 10238-21-8, Glyburide 21187-98-4, Gliclazide 27686-84-6 29094-61-9, Glipizide 56180-94-0, Acarbose 72432-03-2, Miglitol 97322-87-7, Troglitazone 103185-28-0 119584-39-3 119584-40-6
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bisphenolic compds. to treat type II diabetes, and combinations with other agents)

IT 50-99-7, Glucose, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(bisphenolic compds. to treat type II diabetes, and combinations with other agents)

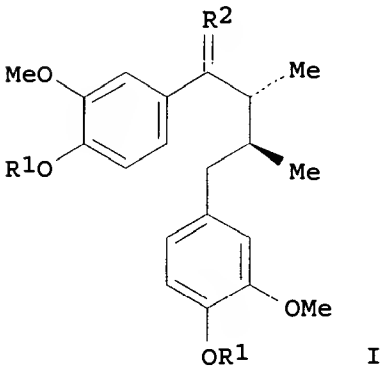
IT 74315-95-0, .alpha.-Glycosidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitors; bisphenolic compds. to treat type II diabetes, and combinations with other agents)

L18 ANSWER 3 OF 17 MARPAT COPYRIGHT 1999 ACS
ACCESSION NUMBER: 126:211905 MARPAT
TITLE: Preparation of cinnamophilin derivatives as platelet aggregation inhibitors, bronchodilators, antioxidants, and vasodilators
PATENT ASSIGNEE(S): National Science Council, Taiwan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09040597	A2	19970210	JP 94-336771	19941213

GI



I

AB The title compds. I [R1 = H, etc.; R2 = O; or C:R2 = CHOH] are claimed. I [R1 = H; R2 = O] (Cinnamophilin) was isolated from Cinnamomum philippinense. Cinnamophilin in vitro showed IC50 of 5.0.+-.0.4 .mu.M against arachidonic acid-induced platelet aggregation.

IC ICM C07C043-23
ICS A61K031-085; A61K031-12; A61K031-22; A61K031-23; A61K035-78; C07C041-34; C07C049-84; C07C069-16; C09K015-08

CC 25-16 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 11

ST cinnamophilin isolation Cinnamomum platelet aggregation inhibitor; Cinnamomum philippinense cinnamophilin isolation; bronchodilator antioxidant vasodilator cinnamophilin

IT Antioxidants
Bronchodilators
Platelet aggregation inhibitors
Vasodilators
(prepn. of cinnamophilin derivs. as platelet aggregation inhibitors, bronchodilators, antioxidants, and vasodilators)

IT Cinnamomum philippinense
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of cinnamophilin derivs. as platelet aggregation inhibitors, bronchodilators, antioxidants, and vasodilators)

IT 154677-96-0P
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(prepn. of cinnamophilin derivs. as platelet aggregation inhibitors, bronchodilators, antioxidants, and vasodilators)

IT 156556-85-3P 187939-69-1P 187939-70-4P 187939-71-5P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cinnamophilin derivs. as platelet aggregation inhibitors, bronchodilators, antioxidants, and vasodilators)

IT 66322-34-7
RL: BOC (Biological occurrence); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(prepn. of cinnamophilin derivs. as platelet aggregation inhibitors, bronchodilators, antioxidants, and vasodilators)

IT 108-24-7, Acetic anhydride 334-88-3, Diazomethane
RL: RCT (Reactant)
(prepn. of cinnamophilin derivs. as platelet aggregation inhibitors, bronchodilators, antioxidants, and vasodilators)

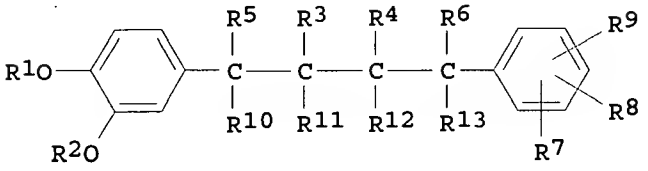
L18 ANSWER 4 OF 17 MARPAT COPYRIGHT 1999 ACS

ACCESSION NUMBER:	125:185864 MARPAT
TITLE:	Treatment of multidrug-resistant cancers with nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs
INVENTOR(S):	Howell, Stephen; Khandwala, Atul; Sachdey, Om P.; Smith, Charles G.
PATENT ASSIGNEE(S):	Chemex Pharmaceuticals, Inc., USA
SOURCE:	U.S., 15 pp. Cont.-in-part of U.S. 5,409,690. CODEN: USXXAM
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5541232	A	19960730	US 94-264740	19940623
US 5409690	A	19950425	US 93-81663	19930623
PRIORITY APPLN. INFO.:			US 93-81663	19930623

GI



I

AB A method and compn. for treating multidrug resistance in a mammal are disclosed, in which the compn. includes NDGA (masoprocol) or a NDGA analog I (R1, R2 = H, lower alkyl, lower acyl; R3-R6, R10-R13 = H, lower alkyl; R7-R9 = H, OH, lower alkoxy, lower acyloxy) in a pharmaceutically acceptable vehicle. The method is particularly suitable for administering an antineoplastic agent, and the compn. includes the combination of NDGA, or an analog with such an antineoplastic agent. Activity of NDGA and a topical formulation contg. NDGA are described.

IC ICM A61K031-045
ICS A61K031-05

NCL 514731000

CC 1-6 (Pharmacology)
Section cross-reference(s): 63

ST nordihydroguaiaretate deriv multidrug resistant cancer treatment

IT Acquired immune deficiency syndrome
(cancers in; nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Antibiotics
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs combined with other antineoplastic compds., and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Biological transport
Neoplasm inhibitors
Pharmaceutical dosage forms
(nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Coordination compounds

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(platinum-contg.; nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs combined with other antineoplastic compds., and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(Hodgkin's disease, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(acute leukemia, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(anus, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Intestine, neoplasm
(anus, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(biliary tract, hepatobiliary; nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(bladder carcinoma, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(central nervous system, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Nervous system
(central, neoplasm, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(chronic leukemia, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(colon, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Intestine, neoplasm
(colon, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Pharmaceutical dosage forms
(emollients, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(endocrine, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(esophagus, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(female reproductive tract, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Reproductive tract
(female, neoplasm, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(head, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Kidney, neoplasm
Lung, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Skin, neoplasm
Stomach, neoplasm
Testis, neoplasm
(inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Pharmaceutical dosage forms
(injections, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(kidney, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(leukemia, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Pharmaceutical dosage forms
(liposomes, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of

multidrug-resistant cancers)
IT Pharmaceutical dosage forms
(liqs., nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
IT Neoplasm inhibitors
(lung, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
IT Neoplasm inhibitors
(lymphocytic lymphoma, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
IT Neoplasm inhibitors
(lymphoma, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
IT Neoplasm inhibitors
(mammary gland, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
IT Thorax
(mediastinum, neoplasm, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
IT Neoplasm inhibitors
(melanoma, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
IT Neoplasm inhibitors
(mesothelioma, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
IT Drug resistance
(multi-, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
IT Neoplasm inhibitors
(neck, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
IT Bladder
(neoplasm, carcinoma, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)
IT Biliary tract
(neoplasm, inhibitors, hepatobiliary; nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Esophagus
Head
Mammary gland
Neck, anatomical
Penis
Prostate gland
Ureter
Urethra
(neoplasm, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Pharmaceutical dosage forms
(ointments, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Pharmaceutical dosage forms
(ointments, creams, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(osteosarcoma, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Bone, neoplasm
(osteosarcoma, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(ovary, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(pancreas, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(penis, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(plasma-cell myeloma, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(prostate gland, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(rectum, nordihydroguaiaretic acid and nordihydroguaiaretic acid

analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Intestine, neoplasm
(rectum, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(skin, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(small intestine, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Intestine, neoplasm
(small, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(soft tissue sarcoma, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Animal tissue
(soft, neoplasm, sarcoma, inhibitors, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Pharmaceutical dosage forms
(solids, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(stomach, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(testis, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(thorax mediastinum, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Pharmaceutical dosage forms
(topical, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Pharmaceutical dosage forms
(transdermal, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of

multidrug-resistant cancers)

IT Neoplasm inhibitors
(ureter, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Neoplasm inhibitors
(urethra, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT Alkaloids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vincaleukoblastine, nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs combined with other antineoplastic compds., and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT 865-21-4, Vinblastine
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs combined with other antineoplastic compds., and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT 15663-27-1, Cisplatin 23214-92-8, Doxorubicin
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs combined with other antineoplastic compds., and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

IT 7440-06-4D, Platinum, coordination complexes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs combined with other antineoplastic compds., and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

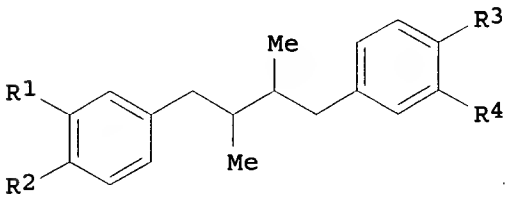
IT 24150-24-1 27686-84-6 36469-60-0 68930-18-7 101432-05-7
103185-28-0 119189-27-4 119189-32-1 119189-33-2 119189-34-3
119189-39-8 119189-40-1 119189-41-2 180634-55-3 180634-56-4
180634-57-5 180634-58-6 180634-59-7 180634-60-0 180634-61-1
180634-62-2 180634-63-3 180634-64-4 180634-65-5 180853-56-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nordihydroguaiaretic acid and nordihydroguaiaretic acid analogs, and pharmaceuticals contg. them, for treatment of multidrug-resistant cancers)

L18 ANSWER 5 OF 17 MARPAT COPYRIGHT 1999 ACS
ACCESSION NUMBER: 125:76343 MARPAT
TITLE: Nordihydroguaiaretic acid derivatives for the suppression of HIV Tat transactivation
INVENTOR(S): Huang, Ru Chih; Gnabbe, John N.
PATENT ASSIGNEE(S): Johns-Hopkins University, USA

SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9610549	A1	19960411	WO 95-US11779	19950922
W: AU, CA, CN, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2200991	AA	19960411	CA 95-2200991	19950922
AU 9536339	A1	19960426	AU 95-36339	19950922
AU 700481	B2	19990107		
EP 783474	A1	19970716	EP 95-933830	19950922
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1162301	A	19971015	CN 95-196035	19950922
JP 10509421	T2	19980914	JP 95-511844	19950922
US 5663209	A	19970902	US 96-627588	19960404
PRIORITY APPLN. INFO.:			US 94-316341	19940930
			WO 95-US11779	19950922

GI



I

AB The invention reveals the isolation, purifn. and characterization from the creosote bush Larrea tridentata of compds. I [R1-R4 = OH, OMe, CH3C(O)O, provided that R1-R4 are not each OH simultaneously]. Each compd. is a deriv. of 1,4-bis(3,4-dihydroxyphenyl)-2,3-dimethylbutane (nordihydroguaiaretic acid, NDGA). In addn., NDGA and each deriv. can be used in a method to suppress Tat transactivation of a lentivirus, including the HIV virus, in a cell by administering NDGA or a deriv. of NDGA to the cell. Fractionation of NDGA derivs. from Larrea tridentata is described. Inhibition of transactivation of HIV promoter activity by NDGA and 4-O-methyl-NDGA was detd.

IC ICM C07C039-12
ICS A61K035-78; A61K031-045

CC 1-5 (Pharmacology)
Section cross-reference(s): 63
ST HIV Tat transactivation inhibition nordihydroguaiaretate deriv; lentivirus Tat transactivation inhibition nordihydroguaiaretate deriv; Larrea nordihydroguaiaretate deriv Tat transactivation inhibition
IT Creosote bush
Virucides and Virustats
(nordihydroguaiaretic acid derivs. from Larrea tridentata for suppression of Tat transactivation of HIV or other lentivirus)
IT Ribonucleic acid formation factors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(gene tat, nordihydroguaiaretic acid derivs. from Larrea tridentata for suppression of Tat transactivation of HIV or other lentivirus)
IT Virus, animal
(human immunodeficiency, nordihydroguaiaretic acid derivs. from Larrea tridentata for suppression of Tat transactivation of HIV or other lentivirus)
IT Virus, animal
(lenti-, nordihydroguaiaretic acid derivs. from Larrea tridentata for suppression of Tat transactivation of HIV or other lentivirus)
IT 500-38-9DP, Nordihydroguaiaretic acid, derivs. 500-38-9P, Nordihydroguaiaretic acid 178557-46-5P
RL: BAC (Biological activity or effector, except adverse); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nordihydroguaiaretic acid derivs. from Larrea tridentata for suppression of Tat transactivation of HIV or other lentivirus)
IT 54473-24-4P 178557-47-6P 178557-48-7P 178557-49-8P 178557-50-1P 178557-51-2P 178557-52-3P 178557-53-4P
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nordihydroguaiaretic acid derivs. from Larrea tridentata for suppression of Tat transactivation of HIV or other lentivirus)

L18 ANSWER 6 OF 17 MARPAT COPYRIGHT 1999 ACS
ACCESSION NUMBER: 122:42331 MARPAT
TITLE: Protective layers for optical polarizer films
INVENTOR(S): Shibue, Toshiaki; Nagayasu, Koichi; Takagi, Tosha
PATENT ASSIGNEE(S): Konishiroku Photo Ind, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 25 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06118233	A2	19940428	JP 92-271879	19921009

GI For diagram(s), see printed CA Issue.

AB The films are from cellulose acetate contg. a UV-absorber I and .gtoreq.1 selected from II, III and IV; in I, Y = H, halo, (substituted) alkyl, alkenyl, alkoxy, phenyl; A = H, alkyl, Ph, cycloalkyl, alkylcarbonyl, alkylcarbonyl, alkylsulfonyl, CO(NH)Dn-1; D = alkyl, alkenyl, (substituted) phenyl; n, m = 1, 2; in II, R1,2 = H, alkyl, alkenyl, aryl; R3,4 = halo, alkyl, cycloalkyl, alkenyl, alkoxy, aryl, aryloxy, alkylthio, arylthio, acyl, acylamino, sulfonyl, sufonylamide, OH; m, n = 0-4; in III, R1 = aliph., aryl; Y = non-metal at. group forming 5-8 heterocyclic ring with N; and in IV, R4 = H, alkyl, cycloalkyl, alkenyl, aryl, heterocyclic group, Si(Ra)(Rb)(Rc); Ra Rb, Rc = alkyl, alkenyl, alkoxy, aryl, alkenoxy, aryloxy, R1-3, R5,6 = H, alkyl, cycloalkyl, alkenyl, aryl, acylamino, sulfonamide, alkylamino, alkylthio, arylthio, alkoxycarbonyl, aryloxycarbonyl, halo, OR7; R4 and R5, R5 and R6, and R1 and R6 may form 5-6-member or spiro rings.

IC ICM G02B005-30
ICS C09K003-00; G02B001-08

CC 73-11 (Optical, Electron, and Mass Spectroscopy and Other Related Properties)

ST polarizer film org protective layer

IT Coating materials
Polarizers
(protective layers for optical polarizer films)

IT 77-08-7 131-54-4 500-38-9 2985-59-3 4673-51-2 6131-38-0 10601-04-4 16181-01-4 76460-83-8 82394-21-6 89929-65-7 116089-83-9 159946-83-5
RL: TEM (Technical or engineered material use); USES (Uses)
(protective layers for optical polarizer films)

L18 ANSWER 7 OF 17 MARPAT COPYRIGHT 1999 ACS

ACCESSION NUMBER: 120:204700 MARPAT
TITLE: Positive-type light-senstitive composition
INVENTOR(S): Yamanaka, Tsukasa; Aoai, Toshiaki; Uenichi, Kazuya; Kondo, Shunichi; Kokubo, Tadayoshi
PATENT ASSIGNEE(S): Fuji Photo Film Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 81 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 541112	A1	19930512	EP 92-119043	19921106
R: BE, DE, FR, GB				
JP 06051519	A2	19940225	JP 92-299093	19921013
PRIORITY APPLN. INFO.:			JP 91-319600	19911108
			JP 92-47705	19920205
			JP 92-47782	19920205
			JP 92-166685	19920603
			JP 92-299093	19921013

AB A pos.-type light-sensitive compn. useful in manuf. of a lithog. plate or a semiconductor device and having less layer shrinkage by baking after exposing, less layer decrease in developing, a good profile, and a high resoln. comprises (a) a resin which is insol. in water and sol. in an alk. aq. soln., (b) a compd. which generates an acid by irradn. with active rays or radial rays, and (c) an acid-decomposable dissoln. inhibitor, having a mol. wt. of not more than 3000 and having groups decomposable by the action of the generated acid to increase the soly. of said inhibitor in an alk. developing soln., wherein said inhibitor (c) is at least one compd. selected from the group consisting of (i) compds. having two of said acid decomposable groups which are sepd. by 10 or more bonded atoms excluding the atoms constituting the acid decomposable groups and (ii) compds. having at least three of said acid decomposable groups and two of said groups which are at the farthest positions are sepd. by 9 or more bonded atoms excluding the atoms constituting the acid decomposable groups.

IC ICM G03F007-004

CC 74-6 (Radiation Chemistry, Photochemistry, and Photographic and Other Reprographic Processes)

ST pos photosensitive compn lithog plate; acid generator pos photosensitive compn

IT Lithographic plates
Semiconductor devices
(manuf. of, pos. photoresist compns. contg. photosensitive acid generators, alkali-sol. resins, and acid-decomposable dissoln. inhibitors for)

IT Phenolic resins, uses
RL: USES (Uses)
(novolak, pos. photoresist compns. contg. photosensitive acid generators, acid-decomposable dessoln. inhibitors and, for lithog. plate and semiconductor device manuf.)

IT Resists
(photo-, pos., contg. photosensitive acid generators, alkali-sol. resins, and acid-decomposable dessoln. inhibitors)

IT 57900-42-2 59626-75-4 62613-15-4 66003-78-9 124737-97-9 142096-70-6 153698-46-5 153698-66-9 153698-67-0
RL: USES (Uses)
(pos. photoresist compn. contg. alkali-sol. resins, acid-decomposable dissoln. inhibitors and, for lithog. plate and

semiconductor device manuf.)

IT 152238-74-9 153698-48-7 153698-49-8 153698-50-1 153698-51-2
153698-52-3 153698-53-4 153698-54-5 153698-55-6 153698-56-7
153698-57-8 153698-58-9 153698-59-0 153698-60-3 153698-61-4
153698-62-5 153698-63-6 153698-64-7 153698-65-8 153840-05-2
RL: USES (Uses)
(pos. photoresist compns. contg. alkali-sol. resins, photosensitive acid generators and, for lithog. plate and semiconductor device manuf.)

IT 24979-70-2, Poly(p-hydroxystyrene) 27029-76-1 112504-03-7
123236-78-2
RL: USES (Uses)
(pos. photoresist compns. contg. photosensitive acid generators, acid-decomposable dessoln. inhibitors and, for lithog. plate and semiconductor device manuf.)

IT 153698-58-9P 153698-68-1P 153698-69-2P 153698-70-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and use of, as acid-decomposable dissoln. inhibitor for pos. photoresist compns.)

IT 110-87-2, 3,4-Dihydro-2H-pyran 865-47-4 4466-18-6 5292-43-3, tert-Butylbromoacetate 24424-99-5, Di-tert-butyldicarbonate 76937-83-2 110726-28-8 153698-47-6
RL: RCT (Reactant)
(reaction of, in prepg. acid-decomposable dissoln. inhibitor for pos. photoresist compns.)

L18 ANSWER 8 OF 17 MARPAT COPYRIGHT 1999 ACS
ACCESSION NUMBER: 119:217422 MARPAT
TITLE: Pharmaceutical compositions containing as active principle associations of vanadium and/or niobium with pyrocatechol derivatives for use in treatment of diabetes and lipid disorders
INVENTOR(S): Maurel, Jean Claude; Kiesgen De Richter, Renaud; Rose, Eric
PATENT ASSIGNEE(S): I.R.2.M., Fr.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9314751	A1	19930805	WO 93-FR68	19930122
W: CA, JP, RU, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2686512	A1	19930730	FR 92-889	19920128

Searcher : Shears 308-4994

FR 2686512 B1 19950630
PRIORITY APPLN. INFO.: FR 92-889 19920128

AB The compns. of the invention contain the assocn. of a mol of a deriv. of vanadium or niobium (oxidn. state 4 or 5) with 1-10 mol of a pyrocatechol deriv. (Markush included). The compns. are useful for the treatment of diabetes, hypercholesterolemia, hypertriglyceridemia, hyperlipidemia, and complications assocd. with these disorders. Prepn. of the compds. of the invention (e.g. a niobium-caffeic acid complex) is described, and the hypoglycemic effect of selected compds. was demonstrated in streptozotocin-treated rats.

IC ICM A61K031-28
ICS A61K033-24
CC 1-10 (Pharmacology)
Section cross-reference(s): 63
ST vanadium pyrocatechol deriv complex antidiabetic; niobium pyrocatechol deriv complex antidiabetic; hypocholesteremic pyrocatechol deriv complex vanadium niobium; hypolipidemic pyrocatechol deriv complex vanadium niobium; hypotriglyceridemic pyrocatechol deriv complex vanadium niobium; caffeic acid niobium complex hypoglycemic
IT Anticholesteremics and Hypolipemics
Antidiabetics and Hypoglycemics
(pyrocatechol deriv. adducts with derivs. of niobium or vanadium)
IT Pharmaceutical dosage forms
(injections, of pyrocatechol deriv. adducts with derivs. of niobium or vanadium, for treatment of diabetes or lipid disorder)
IT Glycerides, biological studies
RL: BIOL (Biological study)
(metabolic disorders, hypertriglyceridemia, treatment of, pyrocatechol deriv. adducts with derivs. of niobium or vanadium for)
IT Pharmaceutical dosage forms
(oral, of pyrocatechol deriv. adducts with derivs. of niobium or vanadium, for treatment of diabetes or lipid disorder)
IT Pharmaceutical dosage forms
(tapes, of pyrocatechol deriv. adducts with derivs. of niobium or vanadium, for treatment of diabetes or lipid disorder)
IT 149-45-1D, Tiron, adducts with derivs. of niobium or vanadium
RL: BIOL (Biological study)
(for treatment of diabetes or lipid disorder)
IT 55-10-7DP, Vanillomandelic acid, reaction products with sodium orthovanadate 90-05-1DP, Guaiacol, reaction products with niobium tetrachloride-THF 108-55-4DP, Glutaric anhydride, reaction products with dihydroxybenzylamine-HBr and vanadyl sulfate 120-80-9DP, Pyrocatechol, derivs., adducts with derivs. of niobium or vanadium 492-89-7DP, 3-Pentadecylcatechol, reaction products with niobium pentaethoxide 500-38-9DP, Nordihydroguaiaretic acid, reaction products with vanadium oxide 501-16-6DP,

trans-3,4-Dihydroxycinnamic acid, reaction products with sodium orthovanadate 530-57-4DP, Syringic acid, reaction products with vanadyl sulfate 1034-01-1DP, Octyl gallate, reaction products with vanadyl sulfate 1314-62-1DP, Vanadium oxide, reaction products with nordihydroguaiaretic acid 3236-82-6DP, Niobium pentaethoxide, reaction products with pentadecylcatechol 7440-03-1DP, Niobium, derivs., adducts with pyrocatechol derivs. 7440-62-2DP, Vanadium, derivs., adducts with pyrocatechol derivs. 10026-12-7DP, Niobium pentachloride, reaction products with dihydroxycinnamic acid 13569-70-5DP, Niobium chloride (NbCl4), reaction products with guaiacol 13569-70-5DP, Niobium tetrachloride, reaction products with hydroxytyramine acid chloride 13718-26-8DP, Sodium metavanadate, reaction products with dihydroxyphenylalanine sodium salt 13721-39-6DP, Sodium orthovanadate, reaction products with pyrocatechol 21092-95-5DP, reaction products with vanadyl sulfate 27774-13-6DP, reaction products with pyrocatechol. 33491-08-6DP, reaction products with vanadyl sulfate 63302-01-2DP, reaction products with sodium metavanadate 63720-39-8DP, reaction products with glutaric anhydride and vanadyl sulfate 150749-73-8DP, reaction products with vanadyl sulfate 150753-35-8DP, reaction products with vanadyl sulfate 150907-50-9DP, reaction products with vanadyl sulfate
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for treatment of diabetes or lipid disorder)

IT 108-55-4, Glutaric anhydride
RL: RCT (Reactant)
(reaction of, with dihydroxybenzylamine-HBr and vanadyl sulfate)

IT 10026-12-7, Niobium pentachloride
RL: RCT (Reactant)
(reaction of, with dihydroxycinnamic acid)

IT 13718-26-8, Sodium metavanadate
RL: RCT (Reactant)
(reaction of, with dihydroxyphenylalanine sodium salt)

IT 63720-39-8, 3,5-Dihydroxybenzylamine hydrobromide
RL: RCT (Reactant)
(reaction of, with glutaric anhydride and vanadyl sulfate)

IT 13569-70-5, Niobium chloride (NbCl4)
RL: RCT (Reactant)
(reaction of, with guaiacol)

IT 13569-70-5, Niobium tetrachloride
RL: RCT (Reactant)
(reaction of, with hydroxytyramine acid chloride)

IT 492-89-7, 3-Pentadecylcatechol
RL: RCT (Reactant)
(reaction of, with niobium pentaethoxide)

IT 90-05-1, Guaiacol
RL: RCT (Reactant)
(reaction of, with niobium tetrachloride-THF)

IT 1314-62-1, Vanadium oxide, reactions

RL: RCT (Reactant)
(reaction of, with nordihydroguaiaretic acid)
IT 3236-82-6, Niobium pentaethoxide
RL: RCT (Reactant)
(reaction of, with pentadecylcatechol)
IT 13721-39-6, Sodium orthovanadate 27774-13-6
RL: RCT (Reactant)
(reaction of, with pyrocatechol)
IT 63302-01-2, 3,4-Dihydroxyphenylalanine sodium salt
RL: RCT (Reactant)
(reaction of, with sodium metavanadate)
IT 55-10-7, Vanillomandelic acid 501-16-6, trans-3,4-Dihydroxycinnamic acid
RL: RCT (Reactant)
(reaction of, with sodium orthovanadate)
IT 500-38-9, Nordihydroguaiaretic acid
RL: RCT (Reactant)
(reaction of, with vanadium oxide)
IT 120-80-9, Pyrocatechol, reactions 530-57-4, Syringic acid 1034-01-1, Octyl gallate 21092-95-5, 3-Benzyloxy-4-hydroxyacetophenone 33491-08-6 150749-73-8 150753-35-8 150907-50-9
RL: RCT (Reactant)
(reaction of, with vanadyl sulfate)
IT 9004-10-8, Insulin, biological studies
RL: BIOL (Biological study)
(resistance, treatment of, pyrocatechol deriv. adducts with derivs. of niobium or vanadium for)

L18 ANSWER 9 OF 17 MARPAT COPYRIGHT 1999 ACS
ACCESSION NUMBER: 119:105755 MARPAT
TITLE: Silver halide color photographic material
INVENTOR(S): Hirabayashi, Shigeto; Yamazaki, Katsumasa
PATENT ASSIGNEE(S): Konica Co., Japan
SOURCE: Eur. Pat. Appl., 108 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 515128	A1	19921125	EP 92-304489	19920518
R: DE, FR, GB, NL				
JP 04346341	A2	19921202	JP 91-147905	19910523
JP 04346344	A2	19921202	JP 91-147908	19910523
JP 05100389	A2	19930423	JP 91-292528	19911011

PRIORITY APPLN. INFO.: JP 91-147905 19910523

JP 91-147908 19910523
JP 91-292528 19911011

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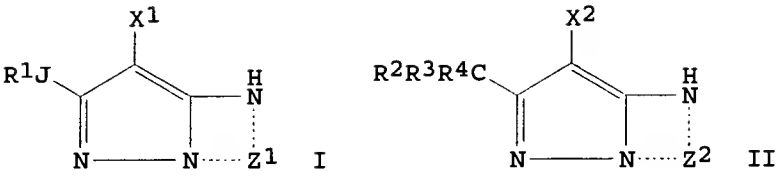

AB A Ag halide color photog. material capable of forming an image of which the characteristic curve ascends with a gentle gradient from the low exposure region to the high exposure region and of forming prints of the same hue irresp. of the type of the printer used comprises 2 kinds of magenta couplers represented by the formulas I and II, resp., (R1 = H, alkyl, or aryl; R2-4 = H, alkyl, or aryl which may combine with each other to form a satd. or unsatd. ring, provided that .gtoreq.2 of them are not H; J = methylene, O or Si X1, X2 = H or a group capable of being released by reaction with an oxidized developing agent; Z1, Z2 = a group of nonmetallic atoms necessary for forming a N-contg. heterocyclic ring which may have a substituent).

IC ICM G03C007-30

CC 74-2 (Radiation Chemistry, Photochemistry, and Photographic and Other Reprographic Processes)

ST pyrazolotriazole magenta photog coupler

IT Photographic emulsions
(color, contg. two kinds of magenta dye formers)

IT Photographic couplers
(magenta, pyrazolotriazoles as)

IT 98155-25-0 104660-19-7 104660-32-4 105343-21-3 109870-77-1 110107-47-6 115007-10-8 115311-14-3 115433-13-1 115773-39-2 117661-36-6 124351-77-5 149042-88-6 149042-89-7 149042-90-0 149042-91-1
RL: TEM (Technical or engineered material use); USES (Uses)
(photog. magenta coupler)

L18 ANSWER 10 OF 17 MARPAT COPYRIGHT 1999 ACS
ACCESSION NUMBER: 116:15811 MARPAT
TITLE: Methods of treating tumors with compositions of catecholic butanes, their preparation, and use of nordihydroguaiaretic acid for tumor inhibition and as a sunscreen agent
INVENTOR(S): Jordon, Russell T.; Neiss, Edward S.; Allen, Larry M.
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA
Searcher : Shears 308-4994

SOURCE: U.S., 11 pp. Cont.-in-part of U.S. Ser. No. 52,120, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5008294	A	19910416	US 87-57481	19870603
CA 1334170	A1	19950131	CA 88-568508	19880602
AU 8817360	A1	19881208	AU 88-17360	19880603
EP 297733	A2	19890104	EP 88-305076	19880603
EP 297733	A3	19901205		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8803957	A	19890222	ZA 88-3957	19880603
JP 01079112	A2	19890324	JP 88-135743	19880603
ES 2020011	A6	19910716	ES 88-1751	19880603
US 5276060	A	19940104	US 91-685609	19910415
AU 9220990	A1	19921008	AU 92-20990	19920813

PRIORITY APPLN. INFO.:
US 79-49886 19790619
US 82-365781 19820405
US 83-465631 19830210
US 84-578501 19840409
US 85-699923 19850211
US 87-52120 19870504
US 87-52420 19870504
US 87-57481 19870603

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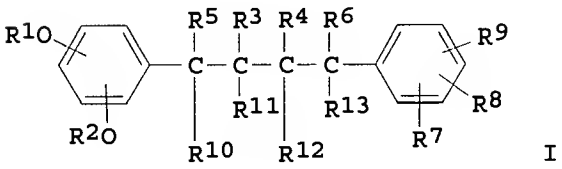

I

AB Catecholic butane derivs. I (R1, R2 = H, lower alkyl, lower acyl, alkylene, R3-R6, R10-R13 = H, lower alkyl; R7-R9 = H, OH, lower alkoxy, lower acyloxy, any 2 adjacent groups together as alkylene dioxy) are provided for treatment of benign, premalignant, and malignant solid tumors, esp. of the skin. Also provided are methods for preventing the occurrence of tumors, and the use of I for sunscreen agents. The preferred I is nordihydroguaiaretic acid (II). Preferred administration methods include topical application and intratumor injection. Prepn. of 1-(3,4-dihydroxyphenyl)-4-

(2,3,4-trihydroxyphenyl)butane is described. II was evaluated in a variety of tumor cell lines and in vivo in mice. A methanolic soln. of II absorbed strongly at 2816 .ANG., a sunlight wavelength known to result in sunburn.

IC ICM A61K031-05
NCL 514731000
CC 1-6 (Pharmacology)
Section cross-reference(s): 25, 62
ST catechol butane deriv antitumor; neoplasm inhibitor catechol butane deriv; sunscreen catechol butane deriv; nordihydroguaiaretic acid antitumor; guaiaretic acid nordihydro antitumor
IT Neoplasm inhibitors
(catecholic butane derivs.)
IT Canis familiaris
Horse
(catecholic butane derivs. as tumor inhibitors for)
IT Sunscreens
(nondihydroguaiaretic acid for)
IT Keratosis
Skin, neoplasm
(treatment of, catecholic butane derivs. for)
IT Keratosis
(actinic, treatment of, catecholic butane derivs. for)
IT Neoplasm inhibitors
(adenocarcinoma, catecholic butane derivs. as, for canine breast adenocarcinoma)
IT Neoplasm inhibitors
(anus adenoma, catecholic butane derivs. as)
IT Intestine, neoplasm
(anus, adenoma, inhibitors, catecholic butane derivs. as)
IT Neoplasm inhibitors
(basal cell carcinoma, catecholic butane derivs.)
IT Skin, neoplasm
(basal cell carcinoma, inhibitors, catecholic butane derivs.)
IT Neoplasm inhibitors
(mast cell carcinoma, catecholic butane derivs.)
IT Neoplasm inhibitors
(melanoma, catecholic butane derivs.)
IT Mammary gland
(neoplasm, adenocarcinoma, treatment of canine, catecholic butane derivs. for)
IT Neoplasm inhibitors
(papilloma, catecholic butane derivs.)
IT Neoplasm inhibitors
(sarcoid, catecholic butane derivs.)
IT Neoplasm inhibitors
(squamous cell carcinoma, catecholic butane derivs.)
IT 3929-47-3P 3945-85-5P, 3-(3,4-Dimethoxyphenyl)propyl bromide
5396-64-5P 81786-49-4P 119189-35-4P 120233-90-1P

138172-13-1P 138172-15-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in catecholic butane deriv. tumor inhibitor prepn.)

IT 119189-34-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for tumor inhibitor)

IT 2103-57-3, 2,3,4-Trimethoxybenzaldehyde 2107-70-2, 3,4-Dimethoxydihydrocinnamic acid
RL: RCT (Reactant)
(reaction of, in catecholic butane deriv. tumor inhibitor prepn.)

IT 500-38-9 5701-82-6 27686-84-6, meso-Nordihydroguaiaretic acid 65987-46-4, 1,4-Bis(3,4-diacetoxyphenyl)-2,3-dimethylbutane 101432-05-7, 1,4-Bis(3,4-dihydroxyphenyl)butane 119189-25-2, 1,4-Bis(3,4-diethoxyphenyl)-2,3-dimethylbutane 119189-26-3, 1,4-Bis(3,4-dipropoxyphenyl)-2,3-dimethylbutane 119189-27-4 119189-28-5 119189-29-6, 1,4-Bis(3,4-dibutyroyloxyphenyl)-2,3-dimethylbutane 119189-30-9, 1,4-Bis(3,4-divaleroyloxyphenyl)-2,3-dimethylbutane 119189-31-0 119189-32-1, 1-(3,4-Dihydroxyphenyl)-4-phenylbutane 119189-33-2, 1-(3,4-Dihydroxyphenyl)-4-(2,5-dihydroxyphenyl)butane 119212-35-0 138172-14-2
RL: BIOL (Biological study)
(tumor inhibitor)

IT 500-38-9
RL: BIOL (Biological study)
(tumor inhibitor and sunscreen)

IT 106-97-8D, Butane, catechol derivs. 120-80-9D, Catechol, butane derivs.
RL: BIOL (Biological study)
(tumor inhibitors)

L18 ANSWER 11 OF 17 MARPAT COPYRIGHT 1999 ACS
ACCESSION NUMBER: 114:69042 MARPAT
TITLE: Preparation of lignan compounds as 5-lipoxygenase inhibitors and aldose reductase inhibitors
INVENTOR(S): Watanabe, Junko; Yanagisawa, Toshihiko; Iketani, Yukinobu; Mihashi, Hiroshi
PATENT ASSIGNEE(S): Tsumura and Co., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 17 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02180846	A2	19900713	JP 88-335305	19881229

Searcher : Shears 308-4994

JP 2754644 B2 19980520

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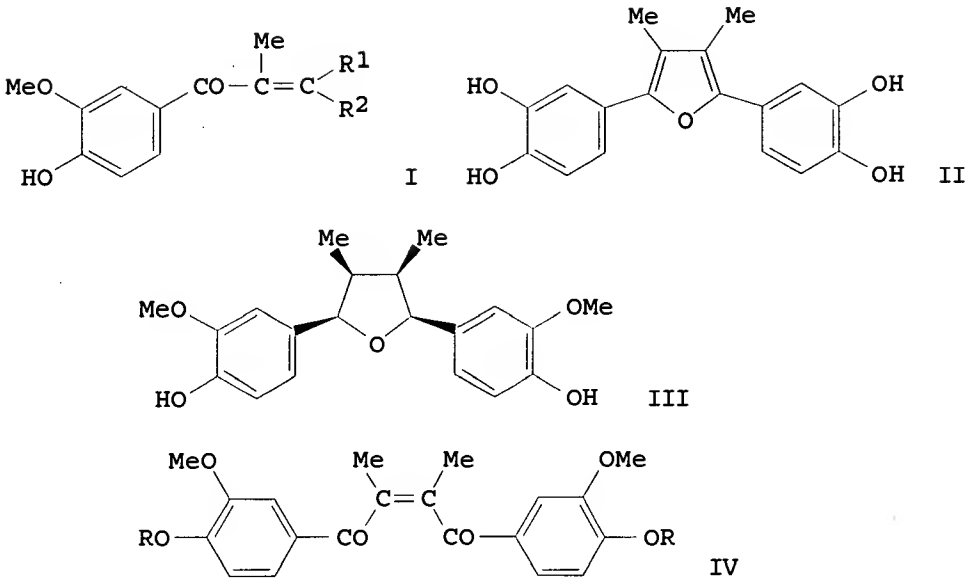

AB Lignan compds. I [R1 = Me, R2 = 4,3-HO(MeO)C8H3CO; R1 = 4,3-HO(MeO)C6H3CO, R2 = Me], II, III, etc., are prepd. for treatment of metab. disorders of arachidonic acid (inflammations, allergy, etc.). Phenolic ketone cis-IV (R = H) (330.7 mg), isolated from Gruaiacum officinale L. resins, was dissolved in DMF and treated with K2CO3 and EtI at room temp. to give 209.2 mg ethered ketone cis-IV (R = Et), which inhibited by 34.6% aldose reductase. The phenolic ketone cis-IV (R = H) showed 99.9% inhibition. Tablet, granular, and injection formulations were given.

IC ICM C07C049-84
ICS A61K031-12; A61K031-34; C07D307-12; C07D307-42

CC 63-4 (Pharmaceuticals)
Section cross-reference(s): 1

ST lignan prepn lipoxygenase inhibitor; aldose reductase inhibitor lignan prepn

IT Ligands
RL: PREP (Preparation)
(prepn. of, as lipoxygenase and aldose reductase inhibitor for treatment of inflammation)

IT 9028-31-3, Aldose reductase 80619-02-9, 5-Lipoxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, ligand derivs. as, for treatment of metab. disorders

of arachidonic acid)
IT 131673-01-3
RL: RCT (Reactant)
(isolation and reaction of, in prepn. of lipoxygenase inhibitors for anti-inflammatory agent)
IT 58096-91-6 131673-02-4 131829-51-1
RL: RCT (Reactant)
(isolation and reaction of, in prepn. of lipoxygenase inhibitors for inflammation treatment)
IT 4676-33-9P 10035-27-5P 10035-28-6P 58096-85-8P 58096-89-2P
66322-34-7P 74683-16-2P 91377-15-0P 114422-21-8P
131673-03-5P
RL: PREP (Preparation)
(prepn. of, as lipoxygenase and aldose reductase inhibitor for treatment of inflammation)

L18 ANSWER 12 OF 17 MARPAT COPYRIGHT 1999 ACS
ACCESSION NUMBER: 111:187581 MARPAT
TITLE: Use of catecholic butanes for the treatment of skin disorders and as neoplasm inhibitors
INVENTOR(S): Neiss, Edward S.; Allen, Larry M.
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 297733	A2	19890104	EP 88-305076	19880603
EP 297733	A3	19901205		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5008294	A	19910416	US 87-57481	19870603
PRIORITY APPLN. INFO.:			US 87-57481	19870603
			US 79-49886	19790619
			US 82-365781	19820405
			US 83-465631	19830210
			US 84-578501	19840409
			US 85-699923	19850211
			US 87-52120	19870504

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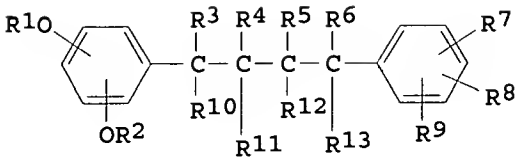


I

AB A pharmaceutical contains .gtoreq.1 catecholic butanes (I; R1, R2 = H, alkyl, lower acyl, alkylene; R3-R6, R10-R13 = H, alkyl; R7-R9 = H, OH, alkoxy, acyloxy, or any adjacent groups together may be alkylenedioxy). 3,4-Dimethoxydihydrocinnamic acid was esterified to give the Me ester which was reduced to give 3-(3,4-dimethoxyphenyl)propanol. The latter was converted to the mesylate which was converted to 3-(3,4-dimethoxyphenyl)propyl bromide which was converted to the Grignard reagent and treated with 2,3,4-trimethoxybenzaldehyde to give 4-(3,4-dimethoxyphenyl)-1-(2,3,4-trimethoxyphenyl)butanol. This was reduced to give 1-(3,4-dimethoxyphenyl)-4-(2,3,4-trimethoxyphenyl)butane, which was demethylated with 48% HBr to give 1-(3,4-dihydroxyphenyl)-4-(2,3,4-trihydroxyphenyl)butane. A preferred I is nordihydroguaiaretic acid (meso isomer) (II). Human mammary carcinoma MX-1 was transplanted to mice and treated intratumorally with a compn. contg. 18.40% by wt. II; after 26 days of treatment the wt. of treated tumors was 17.1% of that of nontreated tumors. Using clonogenic (cancer cell) assays II was found to inhibit the growth of canine breast adenocarcinoma tumor cells, MC-1 equine sarcoid cells, and human lung tumor cell line LX-T. II nearly completely prevented tumor promotion by phorbol ester and reduced tumor promotion by dimethylbenzanthrene in mice. I can also be used to treat acne and other skin disorders, or they can be used as sunscreen agents.

IC ICM A61K031-05
ICS A61K031-085; A61K031-22

CC 1-5 (Pharmacology)
Section cross-reference(s): 25

ST catecholic butane neoplasm inhibitor; nordihydroguaiaretic acid skin disease; acne nordihydroguaiaretic acid; sunscreen nordihydroguaiaretic acid

IT Neoplasm inhibitors
(catecholic butanes)

IT Acne
Skin, disease or disorder
(treatment of, catecholic butanes for)

IT Neoplasm inhibitors
(carcinoma, catecholic butanes)

IT Sunburn and Suntan
(sunscreens, catecholic butanes for)

IT 2103-57-3, 2,3,4-Trimethoxybenzaldehyde

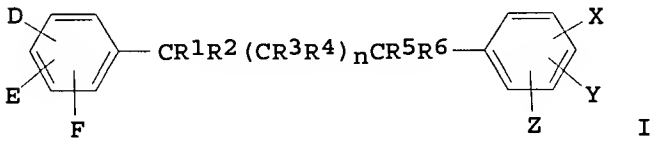
RL: RCT (Reactant)
(Grignard reaction of, with (dimethoxyphenyl)propyl bromide)
IT 2107-70-2, 3,4-Dimethoxydihydrocinnamic acid
RL: PROC (Process)
(conversion of, to Me ester)
IT 500-38-9, 1,4-Bis(3,4-dihydroxyphenyl)-2,3-dimethylbutane
5701-82-6, 1,4-Bis(3,4-dimethoxyphenyl)-2,3-dimethylbutane
27686-84-6, meso-Nordihydroguaiaretic acid 65987-46-4,
1,4-Bis(3,4-diacetoxyphenyl)-2,3-dimethylbutane 101432-05-7
119189-25-2, 1,4-Bis(3,4-diethoxyphenyl-2,3-dimethylbutane
119189-26-3, 1,4-Bis(3,4-dipropoxyphenyl)-2,3-dimethylbutane
119189-27-4 119189-29-6 119189-30-9, 1,4-Bis(3,4-
divaleroyloxyphenyl)-2,3-dimethylbutane 119189-31-0,
1,4-Bis(3,4-dipivaloyloxyphenyl)-2,3-dimethylbutane 119189-32-1,
1-(3,4-Dihydroxyphenyl)-4-phenylbutane 119189-33-2,
1-(3,4-Dihydroxyphenyl)-4-(2,5-dihydroxyphenyl)butane 123292-93-3
RL: BIOL (Biological study)
(neoplasm inhibitor and antiacne agent and sunscreen agent)
IT 3945-85-5P, 3-(3,4-Dimethoxyphenyl)propyl bromide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and Grignard reaction of, with trimethoxybenzaldehyde)
IT 81786-49-4P, 3-(3,4-Dimethoxyphenyl)propyl methanesulfonate
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and conversion of, to bromide)
IT 120233-90-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and demethylation of)
IT 27798-73-8P, Methyl 3,4-dimethoxydihydrocinnamate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydride redn. of)
IT 3929-47-3P, 3-(3,4-Dimethoxyphenyl)propanol
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and mesylation of)
IT 119189-35-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reductive dehydration of)
IT 119189-34-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as neoplasm inhibitor and antiacne agent and
sunscreen agent)

L18 ANSWER 13 OF 17 MARPAT COPYRIGHT 1999 ACS
ACCESSION NUMBER: 111:17704 MARPAT
TITLE: Neoplasm inhibitors comprising metal salts and phenol derivatives
INVENTOR(S): Jordan, Russell T.; Allen, Larry M.
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
Searcher : Shears 308-4994

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8803805	A1	19880602	WO 86-US2547	19861119
W: AU, DK, FI, JP, KP, KR, NO, SU				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8767794	A1	19880616	AU 87-67794	19861119
EP 290442	A1	19881117	EP 87-900420	19861119
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 01501791	T2	19890622	JP 87-500359	19861119
AU 9168662	A1	19910314	AU 91-68662	19910104

PRIORITY APPLN. INFO.: WO 86-US2547 19861119
GI



I

AB Antitumor compns. comprise a metal salt and the phenols I [D, E, F, X, Y, Z = H, OH, (un)substituted alkoxy or acyloxy; R1-R6 = H, (un)substituted alkyl or alkoxy, etc.; n = 0, 1-5; the phenolic groups may be joined by CH2, CH2CH2, HOP(O), R7OP(O); R7 = alkyl; either of the 2 benzene rings may be replaced by cyclohexyl, naphthyl, tetrahydronaphthyl, pyridyl, piperinyl, quinolinyl, indanyl or indenyl; any R4-R6 may be joined with the benzene carbons to form rings]. The metal salts are of Zn, Cr(III), Y, Co(II), Co(III), Ni, Mg, Al, Cu(I), Cu(II), Fe(III), Cd, Sb, Hg, Rb, V, or rare earth metals. 1-(3,4-Dimethoxyphenyl)-4-(2,3,4-trimethoxyphenyl)butane (prepn. given) was refluxed with HBr under N for 9 h to give 1-(3,4-dihydroxyphenyl)-4-(2,3,4-trihydroxyphenyl)butane (II). Intratumor administration of II together with ZnCl2 enhanced the survival time and decreased tumor incidence in mice with transplanted human breast adenocarcinoma. An ointment contained ZnCl2 10.0, a catecholic butane 5.0, PEG-400 4.2, PEG-8000 61.7, water 19.0 and ascorbic acid 0. mg by wt.

IC ICM A61K033-30
ICS A61K031-05
CC 1-6 (Pharmacology)
Section cross-reference(s): 25, 27
ST antitumor metal salt phenol deriv; zinc chloride nordihydroguiaretic

acid antitumor
IT Larrea divaricata
(ext., neoplasm inhibitors contg. metal salts and)
IT Alcohols, biological studies
Aldehydes, biological studies
RL: BIOL (Biological study)
(neoplasm inhibitors contg. metal salts and)
IT Neoplasm inhibitors
(phenolic compd.-metal salt mixts.)
IT Keratosis
(actinic, treatment of, phenolic compd.-metal salt mixt. for)
IT Neoplasm inhibitors
(adenocarcinoma, phenolic compd.-metal salt mixts.)
IT Carboxylic acids, biological studies
RL: BIOL (Biological study)
(aliph., neoplasm inhibitors contg. metal salts and)
IT Skin, neoplasm
(basal cell carcinoma, treatment of, phenolic compd.-metal salt mixt. for)
IT Intestine, neoplasm
(colon, treatment of, phenolic compd.-metal salt mixt. for)
IT Neoplasm inhibitors
(glioma, phenolic compd.-metal salt mixts.)
IT Bactericides, Disinfectants, and Antiseptics
Fungicides and Fungistats
(medical, phenolic compd.-metal salt mixts.)
IT Neoplasm inhibitors
(melanoma, phenolic compd.-metal salt mixts.)
IT Mast cell
(neoplasm, treatment of, phenolic compd.-metal salt mixt. for)
IT Mammary gland
(neoplasm, adenocarcinoma, treatment of, phenolic compd.-metal salt mixt. for)
IT Flavonoids
RL: BIOL (Biological study)
(oxo, neoplasm inhibitors contg. metal salts and)
IT Flavonoids
RL: BIOL (Biological study)
(oxo hydroxy, neoplasm inhibitors contg. metal salts and)
IT Flavonoids
RL: BIOL (Biological study)
(oxo hydroxy methoxy, neoplasm inhibitors contg. metal salts and)
IT Neoplasm inhibitors
(renal cell carcinoma, phenolic compd.-metal salt mixts.)
IT Neoplasm inhibitors
(sarcoid, phenolic compd.-metal salt mixts.)
IT Ulcer inhibitors
(skin, phenolic compd.-metal salt mixts.)
IT Neoplasm inhibitors

(squamous cell carcinoma, phenolic compd.-metal salt mixts.)

IT 2103-57-3, 2,3,4-Trimethoxybenzaldehyde
RL: RCT (Reactant)
(Grignard reaction of, with dimethoxyphenylpropyl bromide)

IT 1835-04-7, 3,4-Dimethoxypropiophenone
RL: BIOL (Biological study)
(condensation of, with bromopropiophenone deriv.)

IT 1835-05-8
RL: BIOL (Biological study)
(condensation of, with propiophenone deriv.)

IT 2107-70-2, 3,4-Dimethoxydihydrocinnamic acid
RL: RCT (Reactant)
(esterification of, with methanol)

IT 113518-66-4 121160-65-4 121160-66-5 121160-67-6 121160-69-8
121160-70-1 121160-71-2 121160-73-4 121160-74-5 121160-75-6
121160-76-7 121160-77-8 121160-78-9 121183-06-0 121202-95-7
121202-96-8
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm inhibitor)

IT 56-53-1D, Diethylstilbestrol, mixts. with metal salts 66-77-3D, 1-Naphthaldehyde, mixts. with metal salts 66-99-9D, 2-Naphthaldehyde, mixts. with metal salts 81-64-1D, Quinizarin, derivs., mixts. with metal salts 81-64-1D, Quinizarin, mixts. with metal salts 88-18-6D, 2-tert-Butylphenol, mixts. with metal salts 88-89-1D, mixts. with metal salts 89-83-8D, Thymol, mixts. with metal salts 90-04-0D, o-Anisidine, mixts. with metal salts 90-18-6D, Quercetagetin, mixts. with metal salts 90-64-2D, Mandelic acid, mixts. with metal salts 91-64-5D, Coumarin, derivs., mixts. with metal salts 92-44-4D, 2,3-Dihydroxynaphthalene, mixts. with metal salts 95-55-6D, 2-Aminophenol, mixts. with metal salts 98-29-3D, 4-tert-Butylcatechol, mixts. with metal salts 98-54-4D, 4-tert-Butylphenol, mixts. with metal salts 99-50-3D, 3,4-Dihydroxybenzoic acid, mixts. with metal salts 102-32-9D, 3,4-Dihydroxyphenylacetic acid, mixts. with metal salts 108-46-3D, 1,3-Benzenediol, derivs., mixts. with metal salts 108-95-2D, Phenol, mixts. with metal salts 110-99-6D, Oxydiacetic acid, mixts. with metal salts 112-53-8D, Lauryl alcohol, mixts. with metal salts 117-39-5D, Quercetin, mixts. with metal salts 118-75-2D, mixts. with metal salts 121-33-5D, Vanillin, mixts. with metal salts 123-31-9D, 1,4-Benzenediol, mixts. with metal salts 123-99-9D, Azelaic acid, mixts. with metal salts 124-04-9D, Hexanedioic acid, mixts. with metal salts 124-13-0D, Octyl aldehyde, mixts. with metal salts 134-01-0D, mixts. with metal salts 139-85-5D, 3,4-Dihydroxybenzaldehyde, mixts. with metal salts 143-07-7D, Lauric acid, mixts. with metal salts 153-18-4D, mixts. with metal salts 154-23-4D, mixts. with metal salts 303-38-8D, 2,3-Dihydroxybenzoic acid, mixts. with metal

salts 315-30-0D, Allopurinol, mixts. with metal salts 331-39-5D, 3,4-Dihydroxycinnamic acid, mixts. with metal salts 437-64-9D, Apigenin 7-methyl ether, mixts. with metal salts 452-86-8D, 4-Methylcatechol, mixts. with metal salts 476-66-4D, derivs., mixts. with metal salts 480-15-9D, Datiscetin, mixts. with metal salts 480-16-0D, Morin, mixts. with metal salts 480-40-0D, Chrysin, mixts. with metal salts 482-35-9D, mixts. with metal salts 491-50-9D, mixts. with metal salts 491-71-4D, Luteolin 3'-methyl ether, mixts. with metal salts 500-38-9D, salts, mixts. with phenolic compds. 500-66-3D, Olivetol, mixts. with metal salts 504-15-4D, Orcinol, mixts. with metal salts 520-18-3D, Kaempferol, mixts. with metal salts 526-75-0D, 2,3-Dimethylphenol, mixts. with metal salts 528-48-3D, Fisetin, mixts. with metal salts 528-53-0D, Delphinidin, mixts. with metal salts 528-58-5D, mixts. with metal salts 529-44-2D, mixts. with metal salts 529-84-0D, 4-Methyl esculetin, mixts. with metal salts 548-83-4D, 3,5,7-Trihydroxyflavone, mixts. with metal salts 552-54-5D, mixts. with metal salts 569-77-7D, Purpurogallin, derivs., mixts. with metal salts 569-77-7D, Purpurogallin, mixts. with metal salts 569-92-6D, Kaempferol 7-methyl ether, mixts. with metal salts 577-85-5D, 3-Hydroxyflavone, mixts. with metal salts 585-34-2D, 3-tert-Butylphenol, mixts. with metal salts 615-94-1D, 2,5-Dihydroxy-p-benzoquinone, mixts. with metal salts 621-82-9D, Cinnamic acid, mixts. with metal salts 643-84-5D, Enidin, derivs., mixts. with metal salts 771-61-9D, Pentafluorophenol, mixts. with metal salts 970-73-0D, Gallocatechin, mixts. with metal salts 1131-62-0D, mixts. with metal salts 1135-24-6D, mixts. with metal salts 1143-38-0D, Dithranol, mixts. with metal salts 1154-78-5D, mixts. with metal salts 1245-15-4D, mixts. with metal salts 1404-00-8D, Mitomycin, mixts. with metal salts 1592-70-7D, Kaempferol 3-methyl ether, mixts. with metal salts 1696-60-2D, Vanillin azine, mixts. with metal salts 2068-02-2D, mixts. with metal salts 2243-27-8D, n-Octyl cyanide, mixts. with metal salts 2896-60-8D, 4-Ethyl resorcinol, mixts. with metal salts 3301-49-3D, Kaempferol 3,7-dimethyl ether, mixts. with metal salts 3943-89-3D, mixts. with metal salts 4382-17-6D, mixts. with metal salts 4440-92-0D, mixts. with metal salts 4650-71-9D, mixts. with metal salts 5507-27-7D, mixts. with metal salts 6068-78-6D, 3,3',4'-Trihydroxyflavone, mixts. with metal salts 6068-80-0D, mixts. with metal salts 6559-91-7D, mixts. with metal salts 6635-20-7D, 5-Nitrovanillin, mixts. with metal salts 7400-08-0D, p-Hydroxycinnamic acid, mixts. with metal salts 7417-21-2D, mixts. with metal salts 7429-90-5D, Aluminum, salts, mixts. with phenolic compds. 7439-89-6D, Iron, salts, mixts. with phenolic compds. 7439-95-4D, Magnesium, salts, mixts. with phenolic compds. 7439-97-6D, Mercury, salts, mixts. with phenolic compds. 7440-02-0D, Nickel, salts, mixts. with phenolic compds. 7440-17-7D, Rubidium, salts, mixts. with phenolic compds. 7440-36-0D, Antimony, salts, mixts. with phenolic compds.

Searcher : Shears 308-4994

7440-43-9D, Cadmium, salts, mixts. with phenolic compds.
7440-47-3D, Chromium, salts, mixts. with phenolic compds.
7440-48-4D, Cobalt, salts, mixts. with phenolic compds.
7440-50-8D, Copper, salts, mixts. with phenolic compds.
7440-62-2D, Vanadium, salts, mixts. with phenolic compds.
7440-65-5D, Yttrium, salts, mixts. with phenolic compds.
7440-66-6D, Zinc, salts, mixts. with phenolic compds. 7646-85-7D, Zinc chloride (ZnCl2), mixts. with phenolic compds. 14414-32-5D, Syringaldazine, mixts. with metal salts 14773-42-3D, mixts. with metal salts 15663-27-1D, Platinum cis-diaminedichloride, mixts. with metal salts 16290-26-9D, 3,4-Dihydroxybenzylamine hydrobromide, mixts. with metal salts 17093-86-6D, 3,3',4',7-Tetramethoxyflavone, mixts. with metal salts 18085-97-7D, 4'-Demethyl eupatilin, mixts. with metal salts 20830-81-3D, Daunomycin, mixts. with metal salts 20869-95-8D, Kaempferol 3,4'-dimethyl ether, mixts. with metal salts 22368-21-4D, Eupatilin, mixts. with metal salts 23820-56-6D, mixts. with metal salts 24289-99-4D, mixts. with metal salts 24677-78-9D, mixts. with metal salts 25739-41-7D, Luteolin 7,3'-dimethyl ether, mixts. with metal salts 27554-19-4D, Kaempferol 3-O-rhamnosylglucoside, mixts. with metal salts 27686-81-3D, mixts. with metal salts 27938-64-3D, mixts. with metal salts 28281-49-4D, mixts. with metal salts 29289-02-9D, mixts. with metal salts 29767-20-2D, VM-26, mixts. with metal salts 33419-42-0D, VP-16, mixts. with metal salts 33708-72-4D, mixts. with metal salts 36469-60-0D, Dihydroguaiaretic acid, mixts. with metal salts 40002-23-1D, 3,4-Dihydrobenzoic acid, mixts. with metal salts 50376-42-6D, Norisoguaiacin, mixts. with metal salts 51487-58-2D, mixts. with metal salts 54375-47-2D, Calcein blue, mixts. with metal salts 56305-02-3D, mixts. with metal salts 65987-46-4D, mixts. with metal salts 68930-19-8D, mixts. with metal salts 68930-20-1D, mixts. with metal salts 69097-99-0D, mixts. with metal salts 70987-96-1D, mixts. with metal salts 86788-60-5D, 3,4',5-Trihydroxyflavone, mixts. with metal salts 94265-62-0D, mixts. with metal salts 100397-63-5D, mixts. with metal salts 101310-77-4D, mixts. with metal salts 101432-05-7D, glycosides, mixts. with metal salts 101432-05-7D, mixts. with metal salts 102454-96-6D, mixts. with metal salts 103185-28-0D, mixts. with metal salts 103239-13-0D, mixts. with metal salts 109202-09-7D, mixts. with metal salts 109202-10-0D, mixts. with metal salts 109697-15-6D, mixts. with metal salts 110420-30-9D, mixts. with metal salts 119189-27-4D, mixts. with metal salts 119189-32-1D, 1-(3,4-Dihydroxyphenyl)-4-phenylbutane, mixts. with metal salts 119189-33-2D, mixts. with metal salts 119189-34-3D, mixts. with metal salts 119189-41-2D, mixts. with metal salts 119584-35-9D, mixts. with metal salts 119773-32-9D, mixts. with metal salts 119773-35-2D, mixts. with metal salts 121152-93-0D, mixts. with metal salts 121152-94-1D, mixts. with metal salts 121152-95-2D, mixts. with metal salts 121152-96-3D,

mixts. with metal salts 121152-97-4D, mixts. with metal salts 121152-98-5D, mixts. with metal salts 121152-99-6D, mixts. with metal salts 121153-00-2D, mixts. with metal salts 121153-01-3D, mixts. with metal salts 121153-02-4D, mixts. with metal salts 121153-03-5D, mixts. with metal salts 121153-04-6D, mixts. with metal salts 121209-88-9D, mixts. with metal salts
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm inhibitors)

IT 3945-85-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and Grignard reaction of, with trimethoxybenzaldehyde)

IT 121153-05-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and Vitride reaction of)

IT 81786-49-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and bromination of)

IT 120233-90-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and deetherification of)

IT 27798-73-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydride redn. of)

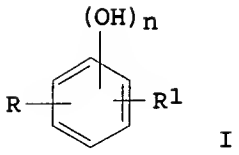
IT 119189-35-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and iodination of)

IT 3929-47-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and mesylation of)

L18 ANSWER 14 OF 17 MARPAT COPYRIGHT 1999 ACS
ACCESSION NUMBER: 110:202685 MARPAT
TITLE: Fogging suppressed silver halide photographic material
INVENTOR(S): Sakamoto, Hidekazu; Ishige, Osamu
PATENT ASSIGNEE(S): Konica Co., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63163337	A2	19880706	JP 86-315775	19861225

GI



I

AB In a photog. material comprising .gtoreq.1 Ag halide emulsion layers, the Ag halide emulsion layer and(or) the adjacent hydrophilic colloid layer(s), contains .gtoreq.1 RSm(CS)nNR1R2 [R = aryl, 5-6-membered heterocyclyl; R1, R2 = H, aliph., arom.; R1 and R2 may join to form a N heterocycle; m = 1, 2; n = 0, 1] and .gtoreq.1 I [n = 2, 3; OH positions are 1,2-, 1,3-, 1,4-, 1,2,3-; R = H, halo, aliph., arom.; R1 = H, aliph., arom., CO2H, CO2M, SO3H, SO3M (M = metal), alkoxycarbonyl, COR2, SO2R2, CONHR3, NHCOR3 (R2, R3 = aliph., arom.]. Fogging during high-temp. development and storage is suppressed.

IC ICM G03C001-34
ICS G03C001-06

CC 74-2 (Radiation Chemistry, Photochemistry, and Photographic and Other Reprographic Processes)

ST fog suppression color film; polyhydroxybenzene fog inhibitor; benzene polyhydroxy fog inhibitor; thiocarbamoyl type fog inhibitor; sulfenamide type fog inhibitor

IT Photographic fog inhibitors
(polyhydroxybenzene and thiocarbamoyl and sulfenamide type)

IT 88-58-4 95-31-8 95-32-9 102-77-2 1166-52-5 2720-65-2 4143-00-4 4568-93-8 24398-42-3 24398-43-4 26773-65-9 29418-16-4 51929-89-6 55605-65-7 60487-86-7 120338-79-6 120338-80-9 120338-81-0 120338-82-1 120338-83-2
RL: USES (Uses)
(photog. fog inhibitors)

L18 ANSWER 15 OF 17 MARPAT COPYRIGHT 1999 ACS
ACCESSION NUMBER: 110:179544 MARPAT
TITLE: Drugs for the treatment of skin disorders and tumors containing catecholic butanes and zinc compounds
INVENTOR(S): Jordan, Russell T.; Allen, Larry M.
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8803806	A1	19880602	WO 86-US2549	19861119
W: AU, DK, FI, JP, KP, KR, NO, SU				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8767379	A1	19880616	AU 87-67379	19861119
PRIORITY APPLN. INFO.:			WO 86-US2549	19861119

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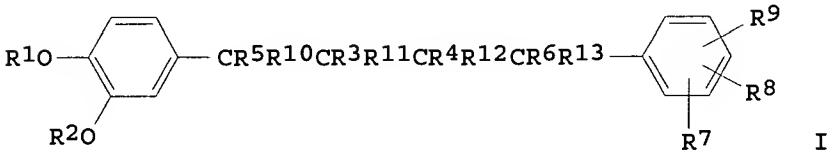


I

AB Compns. comprising the catecholic butanes I (R1, R2 = H, alkyl, acyl; R3, R4, R5, R6, R10, R11, R12, R13 = H, alkyl; R7, R8, R9 = H, OH, alkoxy, acyloxy) and Zn2+ are skin drugs, microbicides and neoplasm inhibitors. 4-(3,4-Dimethoxyphenyl)-1-(2,3,4-trimethoxyphenyl)butanol (prepn. given) was stirred with NaH and MeI in dry DMF, followed by the addn. of H2O and extn. with CHCl3, to give an intermediate (not isolated), which upon reaction with Na in liq. NH3 gave 1-(3,4-dimethoxyphenyl)-4-(2,3,4-trimethoxyphenyl)butane. This was refluxed with HBr under N for 9 h to give 1-(3,4-dihydroxyphenyl)-4-(2,3,4-trihydroxyphenyl)butane. An ointment comprised ZnCl2 10, I 5.0, PEG-400 4.2, PEG-8000 51.7, H2O 19.0 and ascorbic acid 0.1%. Topical application of a compn. contg. 27.5% ZnCl2 and 6.9% nordihydroquaiaretic acid reduced the size or completely suppressed B-16 melanoma and sarcoma-180 tumors in mice, and increased the survival time of the animals.

IC ICM A61K033-30
ICS A61K031-05

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 25

ST catecholic butane zinc anticancer antimicrobial; phenylbutane prepn drug

IT Propionibacterium acnes
Staphylococcus aureus
(bactericide for, catecholic butane- and zinc-contg. compns.)

IT Bactericides, Disinfectants, and Antiseptics
Fungicides and Fungistats
Neoplasm inhibitors
(catecholic butanes- and zinc-contg. drugs)

IT Wound healing
(stimulation of, by drugs contg. catecholic butanes and zinc)

IT Skin, disease or disorder

(treatment of, with catecholic butanes- and zinc-contg. compns.)

IT Acne
Osteomyelitis
(treatment of, with catecholic butanes- and zinc-contg. drugs)

IT 2103-57-3, 2,3,4-Trimethoxybenzaldehyde
RL: RCT (Reactant)
(Grignard reaction of, with (dimethoxyphenyl)propyl bromide)

IT 500-38-9, Nordihydroguaiaretic acid 546-46-3, Zinc citrate 553-72-0, Zinc benzoate 557-09-5, Zinc caprylate 557-34-6, Zinc acetate 4468-02-4, Zinc gluconate 7646-85-7, Zinc chloride, biological studies 7699-45-8, Zinc bromide 7733-02-0, Zinc sulfate 7779-88-6, Zinc nitrate 7779-90-0, Zinc phosphate 10139-47-6, Zinc iodide
RL: BIOL (Biological study)
(antimicrobial and antineoplastic compn. contg., for skin)

IT 112867-79-5 119189-27-4 119189-32-1 119189-33-2 119189-41-2 119189-42-3
RL: BIOL (Biological study)
(antimicrobial and antineoplastic drug, for skin)

IT 2107-70-2
RL: RCT (Reactant)
(esterification of, with methanol)

IT 3945-85-5P
RL: PREP (Preparation); RCT (Reactant)
(prepn. and Grignard reaction of, with trimethoxybenzaldehyde)

IT 81786-49-4P
RL: PREP (Preparation); RCT (Reactant)
(prepn. and bromination of)

IT 103239-13-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and esterification of)

IT 68930-18-7P 120233-90-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrolysis of)

IT 3929-47-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and mesylation of)

IT 103185-27-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of)

IT 4440-92-0P 27798-73-8P 119189-35-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)

IT 103185-28-0P
RL: PREP (Preparation)
(prepn. of, as antimicrobial and antineoplastic drug, for skin)

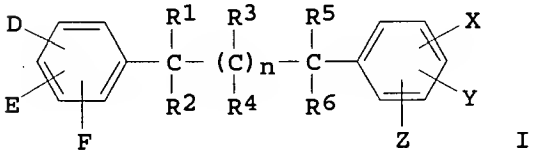
IT 119189-28-5P 119189-31-0P
RL: PREP (Preparation)
(prepn. of, as antimicrobial antineoplastic drug)

IT 119189-34-3P
RL: PREP (Preparation)
(prepn. of, as antineoplastic drug)
IT 1835-04-7, 3,4-Dimethoxypropiophenone
RL: RCT (Reactant)
(reaction of, with bromodimethoxypropiophenone)
IT 1835-05-8
RL: RCT (Reactant)
(reaction of, with dimethoxypropiophenone)

L18 ANSWER 16 OF 17 MARPAT COPYRIGHT 1999 ACS
ACCESSION NUMBER: 110:147880 MARPAT
TITLE: Arachidonic acid lipoxygenase inhibitors for the treatment of psoriasis
INVENTOR(S): Jordan, Russell T.; Allen, Larry M.
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8803800	A1	19880602	WO 86-US2548	19861119
W: AU, BB, DK, JP, KP, KR, NO, SU				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8767375	A1	19880616	AU 87-67375	19861119
EP 289506	A1	19881109	EP 87-900421	19861119
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 01501790	T2	19890622	JP 87-500248	19861119
AU 9068116	A1	19910314	AU 90-68116	19901217
PRIORITY APPLN. INFO.:			WO 86-US2548	19861119

GI



I

AB The enzymic action of the arachidonic acid lipoxygenase is inhibited by the administration of diphenylalkyl derivs. (I; D, E, F, X, Y, Z

= H, OH, optionally substituted alkoxy or acyl; R1-R6 = lower alkyl, alkoxy, substituted amino, carboxyl, carbalkoxyl, OH, CO, aryl, aralkyl; the Ph rings may contain 1-3 substituents comprising OH, alkenoxy, alkyl, alkoxy, substituted amino, carboxy, carbalkoxy, CF3, halo, cyano, CH2OH, SO3H, sulfonamido, NHSO2R, NO2, carbonyloxy, aminocarbonyloxy, aroyloxy, aralkanoyloxy, heteroaryloxy, glycosidyloxy; the phenolic groups may be joined by CH2, CH2CH2, HOPO, alkylOPO, R2NPO). The 50% inhibiting concn. (IC50) for soybean lipoxygenase by 1-(3,4-dihydroxyphenyl)-4-3,5-diaminophenyl)butane was 1.85 .times. 10-4 mol/L. For nordihydroguiaretic acid, a known lipoxidase inhibitor IC50 = 2.9 .times. 10-4 mol/L. Other compds. tested were e.g. 4-propylcatechol, meso nordihydroguaiaretic acid, and Etoposide; for these IC50 were 4.00, 2.60, 2.10 .times. 10-4 mol/L, resp.

IC ICM A61K031-20
ICS A61K031-075; A61K031-045

CC 1-12 (Pharmacology)

ST arachidonic acid lipoxygenase inhibitor psoriasis; catecholic butane psoriasis

IT Tocopherols
RL: BIOL (Biological study)
(arachidonic acid lipoxygenase inhibitor, pharmaceuticals contg., for treatment of psoriasis)

IT Bronchodilators
(arachidonic acid lipoxygenase inhibitors)

IT Uterus
(contractions, inhibition of, with arachidonic acid lipoxygenase inhibitors)

IT Hay fever
Psoriasis
(treatment of, with arachidonic acid lipoxygenase inhibitors)

IT Dermatitis
(allergic, treatment of, with arachidonic acid lipoxygenase inhibitors)

IT Bronchodilators
(antiasthmatics, arachidonic acid lipoxygenase inhibitors, catecholic butanes as)

IT Intestine
(colon, htpercontraction of, inhibition of, with arachidonic acid lipoxygenase inhibitors)

IT Eye, disease or disorder
(conjunctivitis, treatment of, with arachidonic acid lipoxygenase inhibitors)

IT Digestive tract
(disease, gastroenteritis, treatment of, with arachidonic acid lipoxygenase inhibitors)

IT Skin, disease or disorder
(insect bite, treatment of, with arachidonic acid lipoxygenase inhibitors)

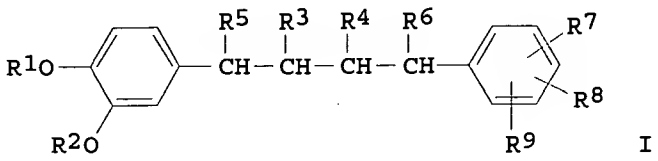
IT 60-10-6, Diphenylthiocarbazone 128-37-0, BHT, biological studies
153-18-4, Rutin 331-39-5, Caffeic acid 500-38-9,
Nordihydroguaiaretic acid 500-38-9D, zinc complexes 518-28-5,
Podophyllotoxin 2525-02-2, 4-Propylcatechol 2896-63-1,
3-Propylcatechol 4375-07-9, Epipodophyllotoxin 5701-82-6
6559-91-7 7440-66-6D, Zinc, NGDA complexes 18085-97-7,
4'-Demethyleupatilin 22368-21-4, Eupatilin 22888-70-6
23077-87-4 27686-84-6 29767-20-2 33419-42-0 40681-80-9
50376-42-6, Norisoguaiacin 56305-04-5, Trolox 59040-30-1,
Nafazatrom 67326-49-2 85129-77-7 86982-61-8 86982-62-9
94265-62-0 119189-27-4 119189-28-5 119189-32-1 119189-33-2
119189-34-3 119584-35-9 119773-32-9 119773-33-0 119773-34-1
119773-35-2 119773-36-3 119789-06-9
RL: BIOL (Biological study)
(arachidonic acid lipoxygenase inhibitor, pharmaceuticals contg.,
for treatment of psoriasis)

IT 63551-74-6, Arachidonic acid lipoxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, catecholic butanes, for treatment of psoriasis)

L18 ANSWER 17 OF 17 MARPAT COPYRIGHT 1999 ACS
ACCESSION NUMBER: 110:141554 MARPAT
TITLE: Pharmacologically active compositions of catecholic butanes with zinc for treatment of skin diseases
INVENTOR(S): Jordan, Russell T.; Allen, Larry M.
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8801509	A1	19880310	WO 86-US1740	19860825
W: AU, DK, FI, GB, JP, NO				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8663304	A1	19880324	AU 86-63304	19860825
PRIORITY APPLN. INFO.:			WO 86-US1740	19860825

GI



I

AB Catecholic butanes I (R1, R2 = alkyl, acyl; R3, R4 = H, Me, Et; R5, R6 = H, OH; R7, R8, R9 = H, OH, OR1) as Zn salts or chelates, or I mixts. with Zn salts, are drugs for the treatment of skin diseases, esp. fungal or bacterial diseases and cancer. A mixt. of ZnCl2 46, meso-1,4-bis(3,4-dihydroxyphenyl)-2,3-dimethylbutane 11.5, quercetin 11.5, Na ascorbate 7.7, solvent 3.0, and polyethylene glycol 20.4% by wt., applied topically twice, controlled B-16 melanoma and S-180 tumor, in mice.

IC ICM A61K033-30
ICS A61K033-24; A61K033-34; A61K033-06; A61K031-05

CC 63-6 (Pharmaceuticals)

ST skin drug catechol butane zinc; neoplasm inhibitor skin catechol zinc

IT Bactericides, Disinfectants, and Antiseptics
Fungicides and Fungistats
Neoplasm inhibitors
(catecholic butane pharmaceuticals contg. zinc as)

IT Wound healing
(enhancement, catecholic butane pharmaceuticals contg. zinc for)

IT Larrea divaricata
Rose
(powd., zinc chloride ext., pharmaceuticals contg., for skin disease treatment)

IT Acne
Osteomyelitis
Skin, disease or disorder
(treatment of, catecholic butane pharmaceuticals contg. zinc for)

IT 136-53-8 546-46-3, Zinc citrate 553-72-0, Zinc benzoate 557-34-6, Zinc acetate 4468-02-4, Zinc gluconate 7440-66-6D, Zinc, salts and chelates 7646-85-7, Zinc chloride, biological studies 7699-45-8, Zinc bromide 7733-02-0, Zinc sulfate 7779-88-6, Zinc nitrate 7779-90-0, Zinc phosphate 10139-47-6, Zinc iodide
RL: BIOL (Biological study)
(pharmaceuticals contg. catecholic butane derivs. and, for skin disease treatment)

IT 500-38-9 5701-82-6 27686-84-6 27686-84-6D, D-glucopyranosyl deriv. and its tetraacetate 65987-46-4 101432-05-7 102454-96-6 103185-28-0 113665-39-7 119189-26-3 119189-27-4 119189-28-5 119189-32-1 119189-33-2 119189-34-3 119189-40-1 119584-34-8

119584-35-9 119584-36-0 119584-37-1 119584-38-2 119584-39-3
119584-40-6 119588-62-4 119607-14-6 119622-63-8
RL: BIOL (Biological study)
(pharmaceuticals contg. zinc salts and, for skin disease treatment)

FILE 'MARPATPREV' ENTERED AT 16:57:31 ON 03 JUN 1999
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS CURRENT RECORDS AND IS UPDATED DAILY
FILE LAST UPDATED: 03 june1999 (19990603/ED)

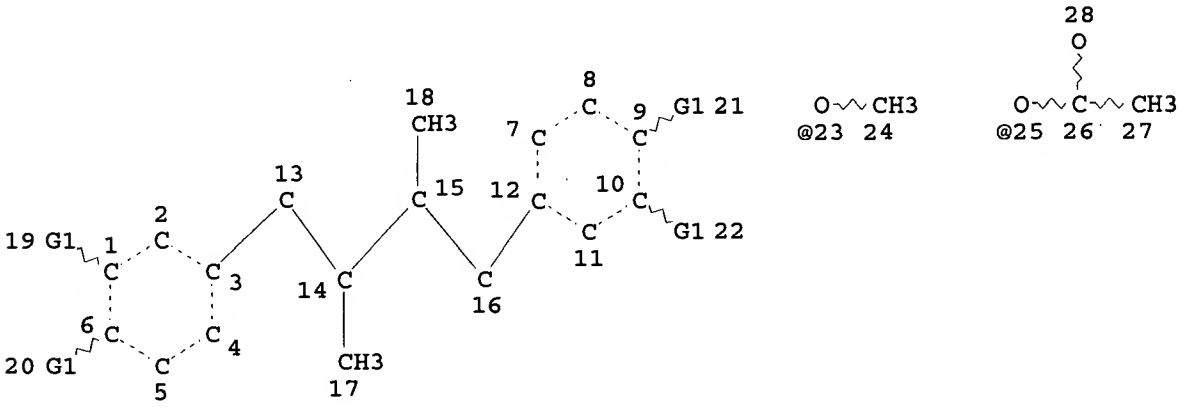
MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US	5905069	18 MAY	1999
DE	19823861	29 APR	1999
EP	913729	06 MAY	1999
JP	11124424	11 MAY	1999
WO	9924873	20 MAY	1999

MARPATprev structure search limits have been raised.
Enter HELP SLIMIT for details.

=> d que stat; fil reg

L5 STR



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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L19 0 SEA FILE=MARPATPREV SSS FUL L5 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 67 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.08

Named compd.

FILE 'REGISTRY' ENTERED AT 16:58:16 ON 03 JUN 1999
E "1,4-BIS-(3,4-DIHYDROXYPHENYL)-2,3-DIMETHYLBUTANE"/CN 5

FILE 'CAPLUS' ENTERED AT 16:58:55 ON 03 JUN 1999
L20 276 SEA ABB=ON PLU=ON BIS(S)(DIHYDROXYPHENYL OR DI(W)(HYDRO XYPHENYL OR HYDROXY(W)(PH OR PHENYL)) OR DIHYDROXY(W)(PH OR PHENYL))
L21 3 SEA ABB=ON PLU=ON L20(S)(DIMETHYLBUTANE OR DI(W)(METHYL BUTANE OR (METHYL OR ME)(W)BUTANE) OR DIMETHYL BUTANE)

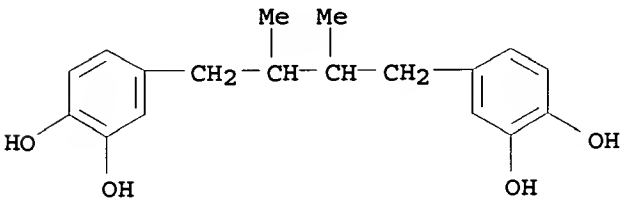
FILE 'REGISTRY' ENTERED AT 17:00:16 ON 03 JUN 1999
E NDGA/CN 5
L22 1 SEA ABB=ON PLU=ON NDGA/CN

=> d l22 ide can

L22 ANSWER 1 OF 1 REGISTRY COPYRIGHT 1999 ACS
RN 500-38-9 REGISTRY
CN 1,2-Benzenediol, 4,4'-(2,3-dimethyl-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Pyrocatechol, 4,4'-(2,3-dimethyltetramethylene)di- (8CI)
OTHER NAMES:
CN .beta.,.gamma.-Dimethyl-.alpha.,.delta.-bis(3,4-dihydroxyphenyl)butane
CN 1,4-Bis(3,4-dihydroxyphenyl)-2,3-dimethylbutane
CN 4,4'-(2,3-Dimethyl-1,4-butanediyl)bis(pyrocatechol)
CN 4,4'-(2,3-Dimethyltetramethylene)dipyrocatechol
CN Butane, 1,4-bis(3,4-dihydroxyphenyl)-2,3-dimethyl-
CN Dihydronorguaiaretic acid
CN Dinorguaiaretic acid, dihydro-
CN **NDGA**
CN Nordihydroguaiaretic acid
CN Norguaiaretic acid, dihydro-
FS 3D CONCORD

Searcher : Shears 308-4994

DR 1413-68-9
MF C18 H22 O4
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CEN, CHEMCATS, CHEMLIST, CBNB, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



938 REFERENCES IN FILE CA (1967 TO DATE)
11 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
938 REFERENCES IN FILE CAPLUS (1967 TO DATE)
17 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 130:287063

REFERENCE 2: 130:276777

REFERENCE 3: 130:276757

REFERENCE 4: 130:261551

REFERENCE 5: 130:246302

REFERENCE 6: 130:233698

REFERENCE 7: 130:232775

REFERENCE 8: 130:193466

REFERENCE 9: 130:148515

REFERENCE 10: 130:123037

=> d his l23- ful; d 1-8 .bevstr

(FILE 'CAPLUS' ENTERED AT 17:01:24 ON 03 JUN 1999)
Searcher : Shears 308-4994

L23 2037 SEA ABB=ON PLU=ON L22 OR NORDIHYDROGUAIARET? OR NOR(W)(DIHYDROGUAIARET? OR DI(W)(HYDROGUAIARET? OR HYDRO GUAIARET?)) OR NORDI(W)(HYDROGUAIARET? OR HYDRO GUAIARET?)
L24 860 SEA ABB=ON PLU=ON NDGA
L25 2264 SEA ABB=ON PLU=ON L23 OR L24
L26 32 SEA ABB=ON PLU=ON L25 AND (VIRAL? OR VIRUS? OR ANTIVIR? OR HERPES? OR (HSV OR HV)(S)HERPES?)
L27 8 SEA ABB=ON PLU=ON (L21 OR L26) NOT L12

L27 ANSWER 1 OF 8 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1994:571626 CAPLUS
DOCUMENT NUMBER: 121:171626
TITLE: Expression of porcine leukocyte 12-lipoxygenase in a baculovirus/insect cell system and its characterization
AUTHOR(S): Reddy, Ramesh Gala; Yoshimoto, Tanihiro; Yamamoto, Shozo; Funk, Colin D.; Marnett, Lawrence J.
CORPORATE SOURCE: Dep. Biochem., Vanderbilt Univ., Nashville, TN, 37232-0146, USA
SOURCE: Arch. Biochem. Biophys. (1994), 312(1), 219-26
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Arachidonate 12-lipoxygenase (12-LO) from porcine leukocytes was expressed in insect cells using a baculovirus expression vector. The recombinant 12-LO was expressed as an N-terminal fusion protein with a 31-amino acid polypeptide carrying a six-histidine tag and an enterokinase cleavage site. Max. intracellular enzyme activity and protein levels were obsd. 48 h after infection of Spodoptera frugiperda cells with the recombinant **virus**. Cells were lysed and the recombinant protein was purified in a single step by Ni2+-nitrilotriacetate column chromatog. The purified enzyme migrated as a single band on sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Recombinant enzyme catalyzed the formation of 12-hydroperoxy-5,8,10,14-eicosatetraenoic acid and a small amt. of 15-hydroperoxy-5,8,11,13-eicosatetraenoic acid. Chiral-phase HPLC anal. indicated that the 12-(S) enantiomer was the predominant product. The purified recombinant 12-lipoxygenase oxygenated linoleic acid to about 19% of the extent of oxygenation of arachidonic acid. **Nordihydroguaiaretic** acid and 5,8,11,14-eicosatetraynoic acid inhibited the recombinant enzyme with IC50's of 2.2 and 0.06 .mu.M, resp. Expression of cloned porcine leukocyte 12-LO in S. frugiperda cells and purifn. by Ni2+-nitrilotriacetate chromatog. provides a straightforward method for isolation of milligram quantities of this form of 12-LO.

L27 ANSWER 2 OF 8 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1993:426488 CAPLUS
DOCUMENT NUMBER: 119:26488
TITLE: Immunomodulation of cellular cytotoxicity to **herpes** simplex **virus** infection in pregnancy by inhibition of eicosanoid metabolism
AUTHOR(S): Feinberg, B. B.; Tan, N. S.; Donovan, P. K.; Loftin, K. C.; Gonik, B.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, USA
SOURCE: J. Reprod. Immunol. (1993), 23(2), 109-18
CODEN: JRIMDR; ISSN: 0165-0378
DOCUMENT TYPE: Journal
LANGUAGE: English

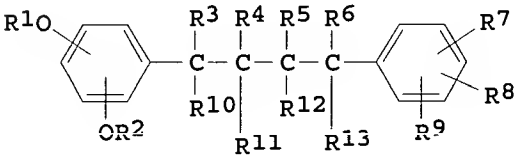
AB In an effort to evaluate the relationships among pregnancy, cellular cytotoxicity and **herpes** simplex **virus** (**HSV**) infection, the authors investigated (1) the maternal cellular cytotoxic response to **HSV** infection as compared with non-pregnant hosts, (2) the influence of both cyclooxygenase and lipoxygenase products on cytotoxicity by selective inhibition of their metabolic pathways, and (3) the potential pregnancy-related differences in immune response to selective inhibition of eicosanoid metab. Indomethacin was used for cyclooxygenase blockade and **nordihydroguaiaretic** acid was used to evaluate lipoxygenase inhibition. In the non-infected animals no differences in cytotoxicity were obsd. between pregnant and non-pregnant groups. HSV infection increased cytotoxicity equally in both groups. Indomethacin did not significantly alter cytotoxicity in either the pregnant or the non-pregnant groups compared with controls. In contrast, **NDGA** elicited a redn. in the cytotoxic response in both pregnant and non-pregnant hosts. Thus, (1) cytotoxicity is maintained at low levels in the absence of HSV infection, (2) HSV infection induces a significant augmentation in host cellular cytotoxicity, (3) pregnant and non-pregnant cytotoxic responses to HSV infection appear comparable, (4) indomethacin does not augment in vitro cytotoxicity to HSV infection and (5) **NDGA** suppresses cytotoxicity, providing evidence that lipoxygenase metabolites are essential to cytotoxic cell function.

L27 ANSWER 3 OF 8 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1989:587581 CAPLUS
DOCUMENT NUMBER: 111:187581
TITLE: Use of catecholic butanes for the treatment of skin disorders and as neoplasm inhibitors
INVENTOR(S): Neiss, Edward S.; Allen, Larry M.
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 297733	A2	19890104	EP 88-305076	19880603
EP 297733	A3	19901205		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5008294	A	19910416	US 87-57481	19870603
PRIORITY APPLN. INFO.:			US 87-57481	19870603
			US 79-49886	19790619
			US 82-365781	19820405
			US 83-465631	19830210
			US 84-578501	19840409
			US 85-699923	19850211
			US 87-52120	19870504

OTHER SOURCE(S): MARPAT 111:187581
GI



I

AB A pharmaceutical contains .gtoreq.1 catecholic butanes (I; R1, R2 = H, alkyl, lower acyl, alkylene; R3-R6, R10-R13 = H, alkyl; R7-R9 = H, OH, alkoxy, acyloxy, or any adjacent groups together may be alkylenedioxy). 3,4-Dimethoxydihydrocinnamic acid was esterified to give the Me ester which was reduced to give 3-(3,4-dimethoxyphenyl)propanol. The latter was converted to the mesylate which was converted to 3-(3,4-dimethoxyphenyl)propyl bromide which was converted to the Grignard reagent and treated with 2,3,4-trimethoxybenzaldehyde to give 4-(3,4-dimethoxyphenyl)-1-(2,3,4-trimethoxyphenyl)butanol. This was reduced to give 1-(3,4-dimethoxyphenyl)-4-(2,3,4-trimethoxyphenyl)butane, which was demethylated with 48% HBr to give 1-(3,4-dihydroxyphenyl)-4-(2,3,4-trihydroxyphenyl)butane. A preferred I is nordihydroguaiaretic acid (meso isomer) (II). Human mammary carcinoma MX-1 was transplanted to mice and treated intratumorally with a compn. contg. 18.40% by wt. II; after 26 days of treatment the wt. of treated tumors was 17.1% of that of nontreated tumors. Using clonogenic (cancer cell) assays II was found to inhibit the growth of canine breast adenocarcinoma tumor cells, MC-1 equine sarcoid cells, and human

lung tumor cell line LX-T. II nearly completely prevented tumor promotion by phorbol ester and reduced tumor promotion by dimethylbenzanthrene in mice. I can also be used to treat acne and other skin disorders, or they can be used as sunscreen agents.

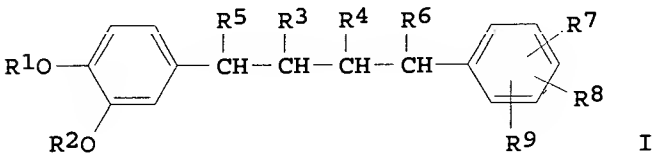
L27 ANSWER 4 OF 8 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1989:210753 CAPLUS
DOCUMENT NUMBER: 110:210753
TITLE: Reversal of **virus**-induced alveolar macrophage bactericidal dysfunction by cyclooxygenase inhibition in vitro
AUTHOR(S): Laegreid, W. W.; Liggitt, H. D.; Silflow, R. M.; Evermann, J. R.; Taylor, S. M.; Leid, R. W.
CORPORATE SOURCE: Dep. Vet. Microbiol., Washington State Univ., Pullman, WA, USA
SOURCE: J. Leukocyte Biol. (1989), 45(4), 293-300
CODEN: JLBIE7; ISSN: 0741-5400
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Virus** infection of alveolar macrophages (AM) both in vivo and in vitro has been assocd. with a decreased ability of these cells to kill bacteria, together with enhanced prodn. of metabolites of arachidonic acid. These metabolites, esp. PGE2, may be inhibitory to some phagocyte functions. Primary cultures of bovine AM obtained by bronchoalveolar lavage of normal cattle were infected in vitro with parainfluenza-3 (PI3 **virus**) **virus**. Killing of Staphylococcus epidermidis by AM was detd. on days 1-4 post-infection (p.i.). PI3 **virus**-infected AM killed significantly fewer bacteria on day 4 p.i. compared to uninfected controls (12.1% infected vs. 52.7% controls). Bacterial killing by **virus**-infected AM, but not control AM, was significantly enhanced on day 4 p.i. by addn. of cyclooxygenase inhibitors 1 h prior to bactericidal assay (28.0% indomethacin, 36.0% mefenamic acid, 38.6% piroxicam, 37.0% **NDGA**, 44.9% ETYA). Phagocytosis of opsonized sheep erythrocytes and superoxide generation by **virus**-infected AM were not significantly increased by cyclooxygenase inhibition. Phagosome-lysosome fusion was severely impaired in **virus**-infected AM. Pretreatment of **virus**-infected AM with indomethacin significantly enhanced the percentage of cell expressing fusion activity. Thus, in vitro bactericidal dysfunction assocd. with **virus** infection of AM is partially the result of enhanced prodn. of prostaglandins or thromboxane by AM and/or an abnormal response to normal levels of endogenously produced cyclooxygenase metabolites. The data further indicate the presence of cyclooxygenase sensitive (phagosome-lysosome fusion) and insensitive (phagocytic) components of **virus**-induced bactericidal dysfunction in AM.

L27 ANSWER 5 OF 8 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER: 1989:141554 CAPLUS
DOCUMENT NUMBER: 110:141554
TITLE: Pharmacologically active compositions of catecholic butanes with zinc for treatment of skin diseases
INVENTOR(S): Jordan, Russell T.; Allen, Larry M.
PATENT ASSIGNEE(S): Chemex Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8801509	A1	19880310	WO 86-US1740	19860825
W: AU, DK, FI, GB, JP, NO				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8663304	A1	19880324	AU 86-63304	19860825
PRIORITY APPLN. INFO.:			WO 86-US1740	19860825

OTHER SOURCE(S): MARPAT 110:141554
GI



I

AB Catecholic butanes I (R1, R2 = alkyl, acyl; R3, R4 = H, Me, Et; R5, R6 = H, OH; R7, R8, R9 = H, OH, OR1) as Zn salts or chelates, or I mixts. with Zn salts, are drugs for the treatment of skin diseases, esp. fungal or bacterial diseases and cancer. A mixt. of ZnCl2 46, meso-1,4-**bis**(3,4-**dihydroxyphenyl**)-2,3-**dimethylbutane** 11.5, quercetin 11.5, Na ascorbate 7.7, solvent 3.0, and polyethylene glycol 20.4% by wt., applied topically twice, controlled B-16 melanoma and S-180 tumor, in mice.

L27 ANSWER 6 OF 8 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1985:540026 CAPLUS
DOCUMENT NUMBER: 103:140026
TITLE: Inhibitors of fatty acid metabolism prevent development of interferon inducing capacity in "aging" chick embryo cells
AUTHOR(S): Sekellick, Margaret J.; Marcus, Philip I.

Searcher : Shears 308-4994

CORPORATE SOURCE: Microbiol. Sect., Univ. Connecticut, Storrs, CT, 06268, USA
SOURCE: Biol. Interferon Syst. Proc. TNO-ISIR Meet. (1985), Meeting Date 1984, 183-7. Editor(s): Kirchner, Holger; Schellekens, Huub. Elsevier: Amsterdam, Neth.
CODEN: 54CNA6
DOCUMENT TYPE: Conference
LANGUAGE: English

AB An interferon inducible state was acquired in primary chick embryo cells as they aged in vitro in the presence of Newcastle disease **virus**. The interferon inducing capacity was prevented by addn. of indomethacin, which inhibited the synthesis of C20 oxygenated fatty acids by blocking the action of fatty acid cyclooxygenase. Other drugs, ibuprofen, aspirin, naproxene, and **nordihydroguaiaretic** acid, which inhibit the synthesis of prostaglandins or leukotrienes also prevented development of interferon inducibility.

L27 ANSWER 7 OF 8 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1985:452608 CAPLUS
DOCUMENT NUMBER: 103:52608
TITLE: Products of the lipoxygenase pathway in human natural killer cell cytotoxicity
AUTHOR(S): Rossi, Paolo; Lindgren, Jan Aake; Kullman, Charlotte; Jondal, Mikael
CORPORATE SOURCE: Dep. Immunol., Karolinska Inst., Stockholm, S-104 01, Swed.
SOURCE: Cell. Immunol. (1985), 93(1), 1-8
CODEN: CLIMB8; ISSN: 0008-8749
DOCUMENT TYPE: Journal
LANGUAGE: English

AB As earlier data suggested the importance of lipoxygenase activation for expression of human natural killer (NK) cell cytotoxicity, 4 different lipoxygenase inhibitors were tested for suppression of NK cell lysis. All inhibitors were active at nontoxic concns., with 50% inhibition at .apprx.15 .mu.M for **nordihydroguaiaretic** acid (**NDGA**). NK cell lysis could be reconstituted in **NDGA**-suppressed cells with leukotriene B4 (LTB4), the all-trans isomers 6-trans-LTB4 and 12-epi-6-trans-LTB4, and 20-carboxyl-LTB4. LTB4 reconstitution was best in the concn. range 1-100 pM and was near control levels at both higher and lower concns. **Herpesvirus** Ateles-transformed killer T cells could also be inhibited by **NDGA**. Lipoxygenase activity is apparently required for human NK cell lysis, and several different LTB4-related products can restore NK activity in inhibited cells; probably the lipoxygenase pathway is present in the killer cell population.

L27 ANSWER 8 OF 8 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1983:437026 CAPLUS
DOCUMENT NUMBER: 99:37026
TITLE: Leukotriene B4 augments human natural cytotoxic cell activity
AUTHOR(S): Rola-Pleszczynski, Marek; Gagnon, Lyne; Sirois, Pierre
CORPORATE SOURCE: Fac. Med., Univ. Sherbrooke, PQ, J1H 5N4, Can.
SOURCE: Biochem. Biophys. Res. Commun. (1983), 113(2), 531-7
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Leukotriene B4 (LTB4) augments human natural cytotoxic lymphocyte activity against target cells infected with **herpes** simplex **virus**. This activity is partially inhibited by the lipoxygenase inhibitor **nordihydroguaiaretic** acid and the thromboxane synthetase inhibitor OKY-1581, but is augmented by the prostaglandin synthesis inhibitor, indomethacin. Thus, LTB4 may play a role in early host defense responses during inflammatory and infectious disease processes.

=> d his l28- ful; d 1-70 ibib abs

(FILE 'MEDLINE, BIOSIS, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT, TOXLIT, TOXLINE, DRUGU, DRUGB, DRUGNL, DRUGLAUNCH, AIDSLINE' ENTERED AT 17:05:19 ON 03 JUN 1999)

L28 6 SEA ABB=ON PLU=ON L21
L29 9584 SEA ABB=ON PLU=ON L23
L30 3981 SEA ABB=ON PLU=ON L24
L31 151 SEA ABB=ON PLU=ON (L29 OR L30) AND (VIRAL? OR VIRUS? OR ANTIVIR? OR HERPES? OR (HSV OR HV)(S) HERPES?)
L32 156 SEA ABB=ON PLU=ON L28 OR L31
L33 78 DUP REM L32 (78 DUPLICATES REMOVED)
L34 17 SEA ABB=ON PLU=ON L31 AND ADMIN?
L35 137 SEA ABB=ON PLU=ON L31 AND (SUPPRESS? OR INHIBIT? OR TREAT? OR THERAP? OR PREVENT?)
L36 143 SEA ABB=ON PLU=ON L28 OR L34 OR L35
L37 70 DUP REM L36 (73 DUPLICATES REMOVED)

L37 ANSWER 1 OF 70 TOXLIT
ACCESSION NUMBER: 1999:14060 TOXLIT
DOCUMENT NUMBER: CA-130-276777U
TITLE: Nontoxic extract of Larrea tridentata, production method, and **therapeutic** use.
AUTHOR: Sinnott RA
SOURCE: (1999). PCT Int. Appl. PATENT NO. 9917609 04/15/1999 (Larreacorp, Ltd.).
CODEN: PIXXD2.

PUB. COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CA
LANGUAGE: English
OTHER SOURCE: CA 130:276777
ENTRY MONTH: 199905

AB A nontoxic, **therapeutic** agent having pharmacol. activity comprising concd. ext. of Larrea tridentata plant material and ascorbic acid is made by a process in which the plant material is extd. using an org. solvent, and is then satd. with ascorbic acid to reduce the toxic **NDGA** quinone, which naturally occurs in the plant material, to **NDGA** itself. Addnl. amts. of ascorbic acid are added to the ext. to **inhibit** the natural oxidn. of the **NDGA** into the toxic **NDGA** quinone in vivo, or during processing or storage. The resulting ext. is useful in the **treatment** of **viral** diseases caused by **viruses** from the **Herpesviridae** family or **viruses** which require the Sp1 class of proteins to initiate **viral** replications. The resulting compd. can also be used as an antiinflammatory when the inflammatory diseases are mediated by the effects of leukotrienes. The listed reducing agents can also be used to stabilize **NDGA** as a **therapeutic** agent or a food additive.

L37 ANSWER 2 OF 70 AIDSLINE
ACCESSION NUMBER: 1998:17463 AIDSLINE
DOCUMENT NUMBER: ICA12-98393903
TITLE: Involvement of chemokine receptors in the induction of interferon by HIV-1.
AUTHOR: Capobianchi M R
CORPORATE SOURCE: Institute For Virology, Rome, Italy.
SOURCE: Int Conf AIDS, (1998). Vol. 12, pp. 273 (Abstract No. 21172).
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICA12
LANGUAGE: English
ENTRY MONTH: 199812

AB BACKGROUND: Persistent activation of the interferon (IFN) system underlies progressing HIV infection. HIV, through its external glycoprotein, induces IFN alpha and gamma in normal PBMC, as a consequence of interaction with both CD4 and galactocerebroside. Additionally, chemokine receptors are involved in HIV infection, mediating **virus** envelope fusion with the target cells. The study was aimed to explore the involvement of chemokine receptors in IFN induction by HIV-1. METHODS: Fixed HIV-1-infected cells were used as IFN inducer in normal PBMC cultures. Newcastle disease **virus** (NDV) was used as conventional **virus** inducer of IFN alpha. Chemokines were used as competitors, and MAbs or

polyclonal antibodies were used as **inhibitors** of membrane interactions involved in IFN induction. Methabolic **inhibitors** were used to block specific signal transduction pathways, either directly or indirectly bound to the chemokine receptor signaling. RESULTS: The alpha-chemokine SDF-1 beta, known to block the infection of T-tropic HIV strains due to interaction with the chemokine receptor CXCR4, **inhibits** IFN induction by HIV-1 IIIB (a T-tropic strain). On the contrary, the beta-chemokines RANTES, MIP1-alpha and -beta, recognizing CCR5, necessary for the infection by monocytotropic HIV, are virually ineffective in the IFN induction by HIV-1 IIIB. Furthermore, the MAb 12G5, and polyclonal antibodies, both recognizing CXCR4, dose-dependently **inhibit** IFN induction by HIV IIIB, and not by NDV. The **inhibitor** of the protein-tyrosin kinase pathway HA, but not PTX, i.e. an **inhibitor** of trimeric G-protein activation, **inhibits** IFN induction by HIV-infected cells. Furthermore, both the cycloxygenase **inhibitor** Indo-M, and the lipoxygenase **inhibitor** **NDGA**, involved in the arachidonate methabolism, are virtually ineffective in IFN induction by HIV. CONCLUSIONS: These results suggest that HIV-1 induces IFN production through unconventional pathways. In fact, the interaction of gp120 with the appropriate chemokine receptor is required, besides CD4 binding, in order to obtain efficient IFN induction by HIV. Furthermore, chemokine receptor driven signal transduction pathway, such as protein-tyrosine kinase activation, seems to be required, while trimeric G-protein activation and arachidonate methabolism seem not to be involved.

L37 ANSWER 3 OF 70 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1998-261002 [23] WPIDS
CROSS REFERENCE: 99-023379 [02]
DOC. NO. CPI: C98-080992
TITLE: Extract of Larrea tridentata with reduced NGDA quinone levels - useful as anti-**viral** and anti-inflammatory agent.
DERWENT CLASS: B04 D13
INVENTOR(S): CLARK, D W; DEBOER, K F; SINNOTT, R A
PATENT ASSIGNEE(S): (LARR-N) LARREACORP LTD
COUNTRY COUNT: 68
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9815184	A1	980416	(9823)*	EN	23

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

AU 9748956 A 980505 (9836)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9815184	A1	WO 97-US18103	971007
AU 9748956	A	AU 97-48956	971007

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9748956	A	Based on	WO 9815184

PRIORITY APPLN. INFO: US 96-726686 961007
AN 1998-261002 [23] WPIDS
CR 99-023379 [02]
AB WO 9815184 A UPAB: 19990113
Method of preparing a non-toxic extract of Larrea tridentata plant material involves: (a) extracting the plant material with a solvent to produce an extract containing **NDGA** (**nordihydroguaiaretic** acid) quinone; (b) filtering the extract; (c) adding an emulsifying and stabilising agent to the extract; (d) reducing the **NDGA** quinone with a compound Q; Q = ascorbic acid (or ester or salt), butylated hydroxyanisole, butylated hydroxytoluene, hydrogen sulphide, hypophosphorous acid monothioglycerol, potassium bisulphite, propyl gallate, sodium bisulphite, sodium hydrosulphite, sodium thiosulphite, sulphur dioxide, sulphurous acid, a tocopherol or vitamin E. Also claimed are pharmaceutical preparations (i) containing **NDGA** and/or Mal.4 (3-0-methyl-**NDGA**) obtained by the above method or (ii) containing **NDGA** and a compound Q.

USE - **NDGA** and Mal.4 are recognised as having **therapeutic** value as anti-**viral**, and anti-inflammatory and anti-cancer agents. Use of extracts of Larrea tridentata for **treatment** has been hampered by the presence of toxic amounts of the **NDGA** quinone in previous preparations. The extracts are also useful as non-toxic food additives to **prevent** oxidation and spoilage.

ADVANTAGE - This method reduces any quinone present and by using additional reducing agents after preparation protects against re-oxidation on storage.

Dwg.0/0

L37 ANSWER 4 OF 70 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-023379 [02] WPIDS
CROSS REFERENCE: 98-261002 [23]
DOC. NO. CPI: C99-007033

Searcher : Shears 308-4994

TITLE: Preparing a composition comprising an extract of Larrea tridentata - extracting Larrea tridentata plant material with acetone, reducing **NDGA** quinone to **NDGA** using ascorbic acid, and concentrating extract.

DERWENT CLASS: B04 D13

INVENTOR(S): CLARK, W D; DEBOER, K F; SINNOTT, R A

PATENT ASSIGNEE(S): (LARR-N) LARREACORP LTD

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5837252	A	981117	(9902)*		11

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5837252	A Provisional	US 96-20946	960701
		US 96-726686	961007

PRIORITY APPLN. INFO: US 96-20946 960701; US 96-726686 961007

AN 1999-023379 [02] WPIDS

CR 98-261002 [23]

AB US 5837252 A UPAB: 19990113

Preparing a composition comprising an extract of Larrea tridentata comprises; (a) harvesting leaves from Larrea tridentata shrubs; (b) air drying the leaves at ambient temperature and humidity for at least 1 week; (c) maintaining the plant material in whole form; (d) extracting the Larrea tridentata extract by recirculating acetone over the plant material at least 3 times to give a Larrea tridentata extract that contains **nordihydroguaiaretic** acid quinone (**NDGA** quinone); (e) filtering particulate impurities from the extract; adding polysorbate 80 (5 ml) to the extract (50 l) as an emulsifying and stabilising agent; (f) reducing the **NDGA** quinone in the extract to NGDA by passing the extract through a column packed with powdered ascorbic acid (5 g ascorbic acid per litre of extract) to reduce the extract; (g) concentrating the reduced extract by 90% by boiling off the reduced acetone solvent at 100 deg. C; (h) adding additional ascorbic acid to **prevent** oxidation of the **NDGA**; and (i) optionally combining the concentrated abstract with carriers, excipients and/or agents.

USE - The extract has anti-inflammatory and **antiviral** activity, e.g. against Hepes (all claimed), particularly against Hepes simplex type 1 (HSV-1), and Kaposi's Sarcoma. **Administration** is topical, formulated as a lotion, or encapsulated.

Searcher : Shears 308-4994

ADVANTAGE - The preparation of the extract minimises the oxidation of **NDGA** to **NDGA** which is toxic.
Dwg.0/5

L37 ANSWER 5 OF 70 TOXLIT
ACCESSION NUMBER: 1998:67471 TOXLIT
DOCUMENT NUMBER: CA-128-275069M
TITLE: Nontoxic **therapeutic** extract of Larrea tridentata.
AUTHOR: Sinnott RA; Clark DW; De Boer KF
SOURCE: (1998). PCT Int. Appl. PATENT NO. 9815184 04/16/1998 (De Boer, Kenneth Frank).
CODEN: PIXXD2.
PUB. COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CA
LANGUAGE: English
OTHER SOURCE: CA 128:275069
ENTRY MONTH: 199805
AB A nontoxic, **therapeutic** agent having pharmacol. activity comprising concd. ext. of Larrea tridentata and a reducing agent, such as ascorbic acid, an ascorbic acid ester, an ascorbic acid salt, butylated hydroxyanisole, butylated hydroxytoluene, hydrogen sulfide, hypophosphorous acid, monothioglycerol, potassium bisulfite, Pr gallate, sodium bisulfite, sodium hydrosulfite, sodium thiosulfate, sulfur dioxide, sulfurous acid, a tocopherol, or vitamin E. The active principle is **nordihydroguaiaretic** acid (**NDGA**). The plant material is extd. using an org. solvent, preferably acetone, and is then satd. with one of the listed reducing agents to reduce the toxic **NDGA** quinone, which naturally occurs in the plant material, to **NDGA** itself. Addnl. amts. of reducing agent may be added to the ext. to **inhibit** the natural oxidn. of the **NDGA** into the toxic **NDGA** quinone in vivo, or during processing or storage. The resulting ext. is useful in the **treatment** of **viral** diseases caused by **viruses** from the **Herpesviridae** family or **viruses** which require the Sp1 class of proteins to initiate **viral** replications. The resulting compd. can also be used as an anti-inflammatory agent when the inflammatory diseases are mediated by the effects of leukotrienes. The listed reducing agents can also be used to stabilize **NDGA** as a **therapeutic** agent or a food additive.

L37 ANSWER 6 OF 70 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1998350158 MEDLINE
DOCUMENT NUMBER: 98350158
TITLE: **Antiviral** activities of methylated **nordihydroguaiaretic** acids. 2. Targeting

herpes simplex virus replication by the mutation insensitive transcription inhibitor tetra-O-methyl-NDGA.

AUTHOR: Chen H; Teng L; Li J N; Park R; Mold D E; Gnabre J; Hwu J R; Tseng W N; Huang R C

CORPORATE SOURCE: Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences, Beijing, China, Organosilicon and Synthesis Laboratory, Department of Chemistry, National Tsing Hua University, Hsinchu, China-Taiwan.

CONTRACT NUMBER: 1 RO1 DE12165 (NIDR)

SOURCE: JOURNAL OF MEDICINAL CHEMISTRY, (1998 Jul 30) 41 (16) 3001-7.
Journal code: J0F. ISSN: 0022-2623.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199810

ENTRY WEEK: 19981004

AB We had previously reported that tetramethyl-O-NGDA (M4N), a synthetic derivative of the naturally occurring nordihydroguaiaretic acid (NDGA), is able to inhibit HIV Tat transactivation by blocking host Sp1 protein at the Sp1 cognate binding site on the HIV LTR promoter. The present studies were undertaken to examine whether M4N is able to inhibit the replication of herpes simplex virus (HSV), another Sp1-regulated virus . The results showed that in Vero cells, M4N inhibits at micromolar levels (IC50 = 43.5 microM) the expression of the herpes immediate early gene (alpha-ICP4), which is essential for HSV replication. An electrophoretic mobility shift assay, examining Sp1 binding to the alpha-ICP4 promoter, showed a significant inhibition of the control bands: 88% inhibition of the fast moving band (FMB) and 45% of the slow moving band (SMB), at 100 microM of drug concentration. Comparative studies between M4N and acycloguanosine (acyclovir, ACV) in cultured Vero cells revealed an interesting pattern in the drug sensitivity (IC50) and cytotoxicity (TC50) parameters. For M4N, the IC50 varied between 11.7 and 4 microM in 10 passages of HSV-1 and 4 passages of HSV-2 with no indication for a requirement of higher drug concentration. In contrast, for acyclovir, the IC50 increased from 7 microM in the first passage to 444 microM in the tenth passage of HSV-1, and >88 microM for the fourth passage of HSV-2, indicating a rapid build-up of drug resistance against acyclovir. While the selective index (SI), defined as the ratio: TC50/IC50, remained relatively constant for M4N; it dropped 60-fold for acyclovir in the endpoints of viral passages. Drug sensitivity for M4N toward the acyclovir-sensitive strain (sm44) and the acyclovir-resistant strain

(ACV-10) of **HSV**-1 was similar, indicating no cross-resistance between M4N and acyclovir in their anti-**HSV** effects. These results may have an important clinical relevance since **HSV** has been shown to be a factor for spreading of HIV.

L37 ANSWER 7 OF 70 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1998350157 MEDLINE
DOCUMENT NUMBER: 98350157
TITLE: **Antiviral** activities of methylated **nordihydroguaiaretic** acids. 1. Synthesis, structure identification, and **inhibition** of tat-regulated HIV transactivation.
AUTHOR: Hwu J R; Tseng W N; Gnabre J; Giza P; Huang R C
CORPORATE SOURCE: Organosilicon and Synthesis Laboratory, Department of Chemistry, National Tsing Hua University, Hsinchu, Taiwan 30043, Republic of China, Institute of Chemistry, Academia Sinica, Nankang, Taipei, Taiwan 11529, Republic of China, and Departmen.
CONTRACT NUMBER: 1 RO1 DE12165 (NIDR)
SOURCE: JOURNAL OF MEDICINAL CHEMISTRY, (1998 Jul 30) 41 (16) 2994-3000.
Journal code: J0F. ISSN: 0022-2623.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199810
ENTRY WEEK: 19981004
AB **Nordihydroguaiaretic** acid (**NDGA**, meso-1) possesses four phenolic hydroxyl groups. **Treatment** of **NDGA** with 0.50-4.1 equiv of dimethyl sulfate and 3.0-6.0 equiv of potassium carbonate in acetone at 56 degrees C gave nine methylated products. Eight of those mono-, di-, tri-, and tetra-O-methylated **NDGAs** were isolated in pure form, and their structures were identified unambiguously by spectroscopic methods. A preparative amount of tetramethyl **NDGA** M4N (10) was obtained in 99% yield from **NDGA** by use of 4.1 equiv of dimethyl sulfate for the methylation. Among the eight different methylated **NDGAs** (2-6 and 8-10), tetra-O-methyl-**NDGA** (10) showed the strongest anti-HIV activity (IC50 11 microM). Chemically synthesized 3'-O-methyl-**NDGA** ((+/-)-2) showed identical anti-HIV activity (IC50 25 microM) to the lignan isolated from Creosote Bush. Lignans with methylated catecholic hydroxyl groups can be produced in large quantities with low cost. At drug concentrations below 30 microM tetramethyl **NDGA** (10) was a stronger anti-HIV agent than mono- and dimethylated **NDGAs**.

L37 ANSWER 8 OF 70 TOXLIT
ACCESSION NUMBER: 1998:136179 TOXLIT
DOCUMENT NUMBER: CA-129-310451Z
TITLE: Human immunodeficiency **virus** type 1 cDNA integration: new aromatic hydroxylated **inhibitors** and studies of the **inhibition** mechanism.
AUTHOR: Farnet CM; Wang B; Hansen M; Lipford JR; Zalkow L; Robinson WEJ; Siegel J; Bushman F
CORPORATE SOURCE: Salk Institute for Biological Studies, La Jolla
SOURCE: Antimicrob. Agents Chemother., (1998). Vol. 42, No. 9, pp. 2245-2253.
CODEN: AMACCQ. ISSN. 0066-4804.
PUB. COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal; Journal Article
FILE SEGMENT: CA
LANGUAGE: English
OTHER SOURCE: CA 129:310451
ENTRY MONTH: 199812

AB Integration of the HIV-1 cDNA is a required step for **viral** replication. Integrase, the **virus**-encoded enzyme important for integration, was not yet exploited as a target for clin. useful **inhibitors**. Here we report on the identification of new polyhydroxylated arom. **inhibitors** of integrase including ellagic acid, purpurogallin, 4,8,12-trioxatricornan, and hypericin, the last of which is known to **inhibit viral** replication. These compds. and others were characterized in assays with subviral preintegration complexes (PICs) isolated from HIV-1-infected cells. Hypericin was found to **inhibit** PIC assays, while the other compds. tested were inactive. Counterscreening of these and other integrase **inhibitors** against addnl. DNA-modifying enzymes revealed that none of the polyhydroxylated arom. compds. are active against enzymes that do not require metals (methylases, a pox **virus** topoisomerase). However, all were cross-reactive with metal-requiring enzymes (restriction enzymes, a reverse transcriptase), implicating metal atoms in the **inhibitory** mechanism. In mechanistic studies, we localized binding of some **inhibitors** to the catalytic domain of integrase by assaying competition of binding by labeled nucleotides. These findings help elucidate the mechanism of action of the polyhydroxylated arom. **inhibitors** and provide practical guidance for further **inhibitor** development.

L37 ANSWER 9 OF 70 SCISEARCH COPYRIGHT 1999 ISI (R)
ACCESSION NUMBER: 1998:298964 SCISEARCH
THE GENUINE ARTICLE: ZG375
TITLE: **Inhibition** of nuclear factor kappa B by direct modification in whole cells - Mechanism of

action of nordihydroguaiaritic acid, curcumin and thiol modifiers
AUTHOR: Brennan P (Reprint); ONeill L A J
CORPORATE SOURCE: IMPERIAL CANC RES FUND, LYMPHOCYTE ACTIVAT LAB, 44 LINCOLNS INN FIELDS, LONDON WC2A 3PX, ENGLAND (Reprint); TRINITY COLL DUBLIN, DEPT BIOCHEM, DUBLIN, IRELAND
COUNTRY OF AUTHOR: ENGLAND; IRELAND
SOURCE: BIOCHEMICAL PHARMACOLOGY, (1 APR 1998) Vol. 55, No. 7, pp. 965-973.
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, ENGLAND OX5 1GB.
ISSN: 0006-2952.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 40

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB This study was set up to investigate the mechanism of four **inhibitors** of interleukin-1 (IL-1)-alpha and tumor necrosis factor-(TNF)alpha activated nuclear factor kappa B (NF kappa B) in whole cells. The compounds fall into two classes: the first comprised two chain-breaking antioxidants, curcumin (diferulolylmethane) and nordihydroguaiaritic acid. The second class were two thiol-modifying agents, N-ethylmaleimide (NEM) and 2-chloro-1,3-dinitrobenzene (CDNB). Both sets of compounds were found to **inhibit** NF kappa B in tumour necrosis factor-activated Jurkat T lymphoma cells and interleukin 1-activated EL4.NOB-1 thymoma cells as determined by electrophoretic mobility shift assay using a specific NF kappa B DNA probe. In unstimulated cells the compounds were found to modify NF kappa B prior to chemical dissociation with sodium deoxycholate. They also **inhibited** DNA binding by NF kappa B when added to nuclear extracts from stimulated cells. Both of these effects occurred over a concentration range comparable to that which **inhibited** cytokine-activated NF kappa B in intact cells. All four agents were found to react directly with the p50 subunit oi NF kappa B. However, only the antioxidants, curcumin and nordihydroguaiaritic acid (**NDGA**) were found to **inhibit** I kappa B alpha degradation activated by tumour necrosis factor-alpha. These results suggest that NF kappa B itself is susceptible to direct **inhibition** by a range of pharmacological agents. Furthermore, curcumin and nordihydroguaiaritic acid **inhibit** NF kappa B by interfering with I kappa B alpha degradation and reacting with p50 in the NF kappa B complex. These findings are likely to be useful in the attempt to develop agents which **inhibit** NF kappa B-dependent gene transcription. (C) 1998 Elsevier Science Inc.

L37 ANSWER 10 OF 70 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1998158730 MEDLINE
DOCUMENT NUMBER: 98158730
TITLE: Retrograde trafficking of both Golgi complex and TGN markers to the ER induced by **nordihydroguaiaretic** acid and cyclofenil diphenol.
AUTHOR: Drecktrah D; de Figueiredo P; Mason R M; Brown W J
CORPORATE SOURCE: Section of Biochemistry, Cornell University, Ithaca, NY 14853, USA.
CONTRACT NUMBER: DK51596 (NIDDK)
SOURCE: JOURNAL OF CELL SCIENCE, (1998 Apr) 111 (Pt 7) 951-65.
Journal code: HNK. ISSN: 0021-9533.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY WEEK: 19981002

AB Previous studies have shown that the Golgi stack and the trans-Golgi network (TGN) may play a role in capturing escaped resident endoplasmic reticulum (ER) proteins, and directing their retrograde transport back to that organelle. Whether this retrograde movement represents a highly specific or more generalized membrane trafficking pathway is unclear. To better understand both the retrograde and anterograde trafficking pathways of the secretory apparatus, we examined more closely the in vivo effects of two structurally unrelated compounds, the potent lipoxygenase **inhibitor nordihydroguaiaretic** acid (**NDGA**), and the non-steroidal estrogen cyclofenil diphenol (CFD), both of which are known to **inhibit** secretion. In the presence of these compounds, transport of vesicular stomatitis **virus** G membrane glycoprotein from the ER to the Golgi complex, and from the TGN to the cell surface, was **inhibited** potently and rapidly. Surprisingly, we found that **NDGA** and CFD stimulated the rapid, but not concomitant, retrograde movement of both Golgi stack and TGN membrane proteins back to the ER until both organelles were morphologically absent from cells. Both **NDGA** - and CFD-stimulated TGN and Golgi retrograde membrane trafficking were **inhibited** by microtubule depolymerizing agents and energy poisons. Removal of **NDGA** and CFD resulted in the complete, but not concomitant, reformation of both Golgi stacks and their closely associated TGN compartments. These studies suggest that **NDGA** and CFD unmask a generalized bulk recycling pathway to the ER for both Golgi and TGN membranes and, further, that **NDGA** and CFD are useful for investigating the molecular mechanisms that control the formation and maintenance of

both the Golgi stack proper and the TGN.

L37 ANSWER 11 OF 70 JICST-EPlus COPYRIGHT 1999 JST
ACCESSION NUMBER: 980372843 JICST-EPlus
TITLE: Protective Effect of Linoleic Acid on IFN .GAMMA.-Induced Cellular Injury in Primary Culture Hepatocytes.
AUTHOR: LIANG J F
AKAIKE T
CORPORATE SOURCE: Tsinghua Univ., Beijing, CHN
Tokyo Inst. Technol., Yokohama
SOURCE: J Biochem, (1998) vol. 123, no. 2, pp. 213-218.
Journal Code: F0286A (Fig. 6, Tbl. 1, Ref. 38)
CODEN: JOBIAO; ISSN: 0021-924X
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
STATUS: New
AB We have previously demonstrated that **treatment** of hepatocytes with IFN .GAMMA. results a series of cellular injury processes, including DNA synthesis arrest, membrane breakage and apoptosis. In the present work, we show that IFN .GAMMA. **suppresses** cellular respiration and protein synthesis in hepatocytes, and that cellular respiration **suppression** is an early event in the IFN .GAMMA.-induced cellular injuries. Polyunsaturated fatty acids (PUFAs) increased cellular respiration of hepatocytes, but only linoleic acid showed some protective effect against IFN .GAMMA.-induced cellular respiration **suppression** . Linoleic acid also reduced other IFN .GAMMA.-mediated cellular injuries, including membrane breakage and protein synthesis **inhibition**. Like linoleic acid, fetal bovine serum also **inhibited** IFN .GAMMA.-induced cellular damage. Increased NAD levels were found in both IFN .GAMMA.-**treated** and non-**treated** hepatocytes following the addition of PUFAs, but clofibrate, a peroxisome proliferator, bromophenacyl bromide (BPB), an **inhibitor** of phospholipase, **nordihydroguaiaretic** acid (**NDGA**), an **inhibitor** of lipoxygenase, and arachidonic acid, a metabolite of linoleic acid, did not **inhibit** IFN .GAMMA.-induced cellular injury. In addition, the combination of linoleic acid and IFN .GAMMA. induced nitric oxide (NO) synthesis in hepatocytes. These results suggest that fatty acid may play an important role in liver homeostasis during chronic inflammatory states and sepsis. (author abst.)

L37 ANSWER 12 OF 70 JICST-EPlus COPYRIGHT 1999 JST
ACCESSION NUMBER: 980504553 JICST-EPlus
TITLE: Involvement of NF-.KAPPA.B activation in the induction of type II nitric oxide synthase in human

glioblastoma cells.
AUTHOR: KOBAYASHI M; SUZUKI T; SUZUKI I; LIOU S-Y; HASHIMOTO Y; HASHIMOTO K
CORPORATE SOURCE: Nippon Glaxo Ltd., Ibaraki, JPN
SOURCE: Biomed Res, (1998) vol. 19, no. 2, pp. 117-126.
Journal Code: Z0236B (Fig. 7, Ref. 52)
ISSN: 0388-6107
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
STATUS: New

AB Nitric oxide (NO) produced by glial cells has been implicated in the pathogenesis of neurodegenerative diseases. In human glial cells, the transcriptional mechanism of inducible NO synthase (iNOS) remains to be understood. We examined the role of the transcription factor NF-.KAPPA.B in the induction of iNOS in a human glioblastoma cell line, A-172. **Treatment** of A-172 cells with lipopolysaccharide (LPS), interleukin-1.BETA.(IL-1.BETA.) and interferon-.GAMMA. (IFN-.GAMMA.) induced iNOS mRNA and protein expression subsequent to the degradation of I.KAPPA.B, a protein that **inhibits** NF-.KAPPA.B, and the DNA binding of NF-.KAPPA.B. Furthermore, the antioxidant pyrroridine dithiocarbamate (PDTC), which is known to **inhibit** NF-.KAPPA.B activation, **inhibited** nitrite production in a dose-dependent manner. The **inhibitory** effect of PDTC correlated with the **prevention** of I.KAPPA.B degradation. Another antioxidant, **nordihydroguaiaretic** acid (**NDGA**), also **inhibited** the nitrite formation and iNOS mRNA expression through its **preventive** effect on NF-.KAPPA.B activation. These results suggest the involvement of NF-.KAPPA.B activation in iNOS induction in human glial cells. (author abst.)

L37 ANSWER 13 OF 70 TOXLINE
ACCESSION NUMBER: 1997:119509 TOXLINE
DOCUMENT NUMBER: BIOSIS-97-20930
TITLE: Clostridium difficile toxin A induces the release of neutrophil chemotactic factors from rat peritoneal macrophages: Role of interleukin-1beta, tumor necrosis factor alpha, and leukotrienes.
AUTHOR: ROCHA M F G; MAIA M E T; BEZERRA L R P S; LYERLY D M; GUERRANT R L; RIBEIRO R A; LIMA A A M
CORPORATE SOURCE: Clinical Res. Unit, Federal Univ. Ceara, PO Box 3229, CEP 60 436-160, Fortaleza, CE, Brazil.
SOURCE: INFECTION AND IMMUNITY, (1997). Vol. 65, No. 7, pp. 2740-2746.
CODEN: INFIBR.
FILE SEGMENT: BIOSIS
LANGUAGE: English

ENTRY MONTH: 199709

AB BIOSIS COPYRIGHT: BIOL ABS. Clostridium difficile produces a potent enterotoxin and cytotoxin, toxins A and B, respectively, which appear to be responsible for pseudomembranous colitis and antibiotic-associated diarrhea. In the present study we explored the neutrophil migration evoked by toxin A in the peritoneal cavities and subcutaneous air pouches of rats and examined the role of macrophages and their inflammatory mediators in this process. Toxin A causes a significant dose-dependent neutrophil influx into the peritoneal cavity, with a maximal response at 0.1 mug/ml and at 4 h. The depletion of macrophages by peritoneal washing **prevents** the toxin A-induced neutrophil migration into the peritoneal cavity. In contrast, an increase in macrophages induced by peritoneal injection of thioglycolate amplifies this toxin effect on neutrophil migration. Furthermore, the injection of supernatants from toxin A-stimulated macrophages into the rat peritoneal cavity causes significant neutrophil migration. Pretreatment of rats with BWA4C, **nordihydroguaiaretic** acid, mepacrine, or dexamethasone **inhibits** the neutrophil migration evoked by toxin A in the peritoneal cavities. However, pretreatment with the cyclooxygenase **inhibitor** indomethacin or the platelet-activating factor antagonist BN52021 fails to alter toxin A-induced neutrophil migration. Toxin A was also injected into air pouches of normal rats or rats pretreated with anti-interleukin-1beta (anti-IL-1beta) or anti-tumor necrosis factor alpha (anti-TNF-alpha) antibodies. Anti-TNF-alpha or anti-IL-1beta antibodies significantly reduce the neutrophil migration induced by toxin A. These data suggest that neutrophil migration evoked by toxin A is in part dependent on macrophage-derived cytokines, such as TNF-alpha and IL-1beta, and leukotrienes. These mediators may help to explain the intense inflammatory colitis caused by C. difficile toxin A in an experimental animal model of this disease.

L37 ANSWER 14 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 97242020 EMBASE

DOCUMENT NUMBER: 1997242020

TITLE: Dermatologic drugs, pregnancy, and lactation: A conservative guide.

AUTHOR: Reed B.R.

CORPORATE SOURCE: Dr. B.R. Reed, 2200 E 18th Ave, Denver, CO 80206, United States

SOURCE: Archives of Dermatology, (1997) 133/7 (894-898).
Refs: 38
ISSN: 0003-987X CODEN: ARDEAC

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 010 Obstetrics and Gynecology
013 Dermatology and Venereology
037 Drug Literature Index

Searcher : Shears 308-4994

038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB No database for determination of precise risk of drug use during pregnancy and lactation is available. There are, however, educated opinions concerning the advisability of use of a drug during the childbearing years from manufacturers, the Food and Drug **Administration**, various teratologists, the American Academy of Pediatrics, and the World Health Organization. Not all medications are absolutely contraindicated during pregnancy and lactation. Some drugs have been extensively used without apparent adverse effects in the mother or infant. When it is necessary to select a medication for use during pregnancy or lactation, the medication should have minimal risk. This article summarizes dermatologic drugs whose known risk is low.

L37 ANSWER 15 OF 70 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 97184665 MEDLINE
DOCUMENT NUMBER: 97184665
TITLE: Activation of the NF-kappaB transcription factor in a T-lymphocytic cell line by hypochlorous acid.
AUTHOR: Schoonbroodt S; Legrand-Poels S; Best-Belpomme M; Piette J
CORPORATE SOURCE: Laboratory of Virology, Institute of Pathology B23, University of Liege, Belgium.
SOURCE: BIOCHEMICAL JOURNAL, (1997 Feb 1) 321 (Pt 3) 777-85. Journal code: 9YO. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199705
ENTRY WEEK: 19970503
AB Reactive oxygen species (ROS) such as hydrogen peroxide serve as second messengers in the induction of the transcription factor NF-kappaB, and hence in the activation and replication of human immunodeficiency **virus** type 1 (HIV-1) in human cells. During inflammatory reactions, many oxidative species are produced, one of which is hypochlorous acid (HOCl), which is responsible for the microbicidal effects of activated human polymorphonuclear leukocytes. **Treatment** of a T-lymphocytic cell line with micromolar concentrations of HOCl promoted the appearance of transcription factor NF-kappaB (the heterodimer p50/p65) in the nucleus of the cells, even in the absence of de novo protein synthesis. Western blot analysis of the NF-kappaB **inhibitory** subunits (IkappaB) demonstrated that both IkappaB-alpha proteolysis and p105 processing were induced by the **treatment**. NF-kappaB activation was very effective when cells were subjected to hyperthermia before being **treated** with HOCl. Various

antioxidants, such as pyrrolidine dithiocarbamate, p-bromophenacyl-bromide and **nordihydroguaiaretic** acid could strongly reduce NF-kappaB translocation, demonstrating the importance of oxidative species in the transduction mechanism. Moreover, ACH-2 cells **treated** with HOCl or H2O2 released tumour necrosis factor-alpha (TNF-alpha) in the supernatants. The importance of TNF-alpha release in NF-kappaB induction by HOCl or H2O2 was demonstrated by the fact that: (1) the nuclear appearance of NF-kappaB was promoted in untreated cells; and (2) synergism between TNF-alpha and HOCl was detected. Collectively, these results suggest that HOCl should be considered as an oxidative species capable of inducing NF-kappaB in a T-lymphocytic cell line through a transduction mechanism involving ROS, and having a long-distance effect through subsequent TNF-alpha release.

L37 ANSWER 16 OF 70 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 97-19242 DRUGU P
TITLE: Biological activity of magnolol: a review.
AUTHOR: Sarker S D
CORPORATE SOURCE: Univ.Exeter
LOCATION: Exeter, U.K.
SOURCE: Fitoterapia (68, No. 1, 3-8, 1997) 1 Fig. 1 Tab. 43 Ref.
CODEN: FTRPAE ISSN: 0367-326X
AVAIL. OF DOC.: Department of Biological Sciences, University of Essex, Washington Singer Laboratories, Perry Road, Exeter, Devon, EX4 4QG, England.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 97-19242 DRUGU P
AB The biological activity of magnolol (MG) is reviewed. MG is a CNS depressant and muscle relaxant, and has antiplatelet, antitumor, insecticidal, antioxidant and antimicrobial actions. MG **inhibits** sperm motility and carrageenan- (CG) and arachidonic acid- (AA) induced 5-HT release from platelets, and **inhibits** tetradecanylphorbolacetate- (TPA) induced papilloma formation. MG **inhibits** CG-induced paw edema and acetic acid- (AC) induced writhing. MG reduces A23187-induced pleurisy and copper sulfate pentahydrate- (CSP) induced emesis. Indomethacin (IN), honokiol (HK), dexamethasone (DM), monoterpentylmagnolol (MM), Saiboku-To (ST), glycyrrhizin (GL), metergoline (MT), tocopherol (TC), **nordihydroguaiaretic** acid (NA), propranolol (PP), cyproheptadine (CH) and tetrodotoxin (TTX) are all mentioned.
ABEX MG is a potent CNS depressant and has muscle relaxant activity. MG has antimicrobial and antiplatelet activity and is a Ca2+ blocker. MG, HK and MM **inhibit** Epstein-Barr **virus** early

antigen activation on Raji cells induced by TPA. MG **inhibits** mouse skin tumor promotion in an in-vivo 2-stage carcinogenesis test. MG applied before TPA delayed papilloma formation in mouse skin. While tail bleeding time of mice is prolonged by MG, it does not **prevent** acute thromboembolic death in mice. MG **inhibits** CG-and AA-induced 5-HT release from platelet suspension. MG **inhibits** CG-induced mouse hind-paw edema and AC-induced writhing. MG reduces the lethality of endotoxin challenge and recovers myeloperoxidase activity in edematous paw but is less effective than IN. Unlike DM, MG does not increase liver glycogen levels. MG reduces A23187-induced protein leakage and PMN infiltration in a mouse pleurisy model. MG appears to be responsible for the antiasthmatic effects of ST. MG is less potent than GL as an **inhibitor** of 11beta-hydroxysteroid dehydrogenase. In isolated rat heart mitochondria, MG and HK are more potent antioxidants than TC. MG **inhibits** UV-induced mutagenesis, and **inhibits** the emetic action of CSP in frogs. MG and HK are more effective than NA in **inhibiting** the acetyltransferase activity in rat spleen microsomes and membrane fractions of human PMN. MG and HK **inhibit** A23187-induced PAF production in human PMN. MG **inhibits** K+-stimulated 5-HT release from rat cortex, effects unchanged by MT, PP, CH or TTX. MG **inhibits** lipid peroxidation in sperm. (RPG)

L37 ANSWER 17 OF 70 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1996-209296 [21] WPIDS
DOC. NO. CPI: C96-066743
TITLE: New 1,4-**Bis**-(3,4-**di** **hydroxyphenyl**)-2,3-**di** **methyl-butane** derivs. - are isolated from extracts of creosote bush, useful for suppressing Tat transactivation of a lentivirus, including HIV.
DERWENT CLASS: B05
INVENTOR(S): GNABRE, J N; HUANG, R; HUANG, R C C; HUANG, R C
PATENT ASSIGNEE(S): (UYJO) UNIV JOHNS HOPKINS
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9610549	A1	960411	(9621)*	EN	61
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: AU CA CN JP					
AU 9536339	A	960426	(9631)		
EP 783474	A1	970716	(9733)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
US 5663209	A	970902	(9741)		17

JP 10509421 W 980914 (9847) 45
AU 700481 B 990107 (9913)

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9610549	A1		WO 95-US11779	950922
AU 9536339	A		AU 95-36339	950922
EP 783474	A1		EP 95-933830	950922
			WO 95-US11779	950922
US 5663209	A	Div ex	US 94-316341	940930
			US 96-627588	960404
JP 10509421	W		WO 95-US11779	950922
			JP 96-511844	950922
AU 700481	B		AU 95-36339	950922

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9536339	A	Based on	WO 9610549
EP 783474	A1	Based on	WO 9610549
JP 10509421	W	Based on	WO 9610549
AU 700481	B	Previous Publ.	AU 9536339
		Based on	WO 9610549

PRIORITY APPLN. INFO: US 94-316341 940930; US 96-627588 960404
AN 1996-209296 [21] WPIDS
AB WO 9610549 A UPAB: 19970516
1,4-**Bis**-(3,4-**dihydroxyphenyl**)-2,3-**dimethyl-butane** derivs. of formula (I) are new: R1-R4 = OH, OMe or OC(O)Me, provided that not all are OH. Also claimed is a method for suppressing Tat transactivation of a lentivirus comprising the admin. to a cell of extracts of Larrea tridentata having the gas chromatography profiles shown in the specification.

USE - (I) and 1,4-**bis**-(3,4-**dihydroxyphenyl**)-2,3-**dimethylbutane** are useful for suppressing Tat transactivation of a lentivirus (claimed), including the HIV virus.

ADVANTAGE - Extract of Larrea tridentata also inhibits HIV cytopathic effects on human lymphoblastoid cells chronically infected with the virus.

Dwg.0/7
ABEQ US 5663209 A UPAB: 19971013
A method for the suppression of Tat transactivation of a lentivirus in a cell comprising the steps of: (a) administering to the cell an effective amount of a compound of formula (I); and (b) allowing the compound to suppress Tat transactivation of the lentivirus in the

cell.
Dwg.0/7

L37 ANSWER 18 OF 70 TOXLIT
ACCESSION NUMBER: 1996:118626 TOXLIT
DOCUMENT NUMBER: CA-125-076343J
TITLE: **Nordihydroguaiaretic** acid derivatives for the **suppression** of HIV Tat transactivation.
AUTHOR: Huang RC; Gnabbe JN
SOURCE: (1996). PCT Int. Appl. PATENT NO. 96 10549 04/11/96 (Johns-Hopkins University).
PUB. COUNTRY: United States
DOCUMENT TYPE: Patent
FILE SEGMENT: CA
LANGUAGE: English
OTHER SOURCE: CA 125:76343
ENTRY MONTH: 199609
AB The invention reveals the isolation, purifn. and characterization from the creosote bush Larrea tridentata of compds. I [R1-R4 = OH, OMe, CH3C(O)O, provided that R1-R4 are not each OH simultaneously]. Each compd. is a deriv. of 1,4-**bis**(3,4-**dihydroxyphenyl**)-2,3-**dimethylbutane** (**nordihydroguaiaretic** acid, **NDGA**). In addn., **NDGA** and each deriv. can be used in a method to **suppress** Tat transactivation of a lentivirus, including the HIV **virus**, in a cell by **administering** **NDGA** or a deriv. of **NDGA** to the cell. Fractionation of **NDGA** derivs. from Larrea tridentata is described. **Inhibition** of transactivation of HIV promoter activity by **NDGA** and 4-O-methyl-**NDGA** was detd.

L37 ANSWER 19 OF 70 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 96389991 MEDLINE
DOCUMENT NUMBER: 96389991
TITLE: **Inhibition** of vesicle-mediated protein transport by **nordihydroguaiaretic** acid.
AUTHOR: Tagaya M; Henomatsu N; Yoshimori T; Yamamoto A; Tashiro Y; Mizushima S
CORPORATE SOURCE: School of Life Science, Tokyo University of Pharmacy and Life Science.
SOURCE: JOURNAL OF BIOCHEMISTRY, (1996 May) 119 (5) 863-9. Journal code: HIF. ISSN: 0021-924X.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
AB **Nordihydroguaiaretic** acid (**NDGA**) blocks intra-Golgi protein transport in a cell-free system and prolactin

secretion from GH3 cells [Tagaya, M., Henomatsu, N., Yoshimori, T., Yamamoto, A., Tashiro, Y., and Fukui, T. (1993) FEBS Lett. 324, 201-204]. To determine which intracellular secretory pathway(s) is **inhibited** by **NDGA**, we investigated its effect on the transport of the vesicular stomatitis **virus**-encoded glycoprotein in BHK-21 cells. **NDGA** blocked protein transport from the endoplasmic reticulum to the Golgi apparatus, and from the trans-Golgi network to the plasma membrane. In addition, it retarded the brefeldin A-induced retrograde transport of mannosidase II to the endoplasmic reticulum. Although **NDGA** had an **inhibitory** effect on protein synthesis, it induced the expression of BiP, a chaperone located in the endoplasmic reticulum. The induction of BiP may be a consequence of the **inhibition** of protein transport by **NDGA**.

L37 ANSWER 20 OF 70 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 96-04638 DRUGU M A
TITLE: Isolation of anti-HIV-1 lignans from Larrea tridentata by counter-current chromatography.
AUTHOR: Gnabre J N; Ito Y; Ma Y; Huang R C
CORPORATE SOURCE: Univ.Johns-Hopkins; Nat.Inst.Health-Bethesda
LOCATION: Baltimore; Bethesda, Md., USA
SOURCE: ; J.Chromatogr. (719, No. 2, 353-64, 1996) 10 Fig. 1 Tab. 26 Ref.
CODEN: ; JOCR
AVAIL. OF DOC.: Department of Biology, The Johns Hopkins University, 144 Mudd Hall, 3400 N. Charles Street, Baltimore, MD 21218-2685, U.S.A. (R.C.H.).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 96-04638 DRUGU M A
AB The results of this paper indicate that the desert creosote bush, Larrea tridentata, is a source for new lignans with anti-HIV activity. These compounds **inhibited** Tat-induced transactivation, being the first plant-derived agents to do so. A powerful bioassay, involving constructs of HIV LTR promotor and reporter gene, the secreted alkaline phosphatase (Seap) and CMV promotor-driven Tat, was established for screening potential HIV **inhibitors**. Counter-current chromatography (CCC) was used to isolate several lignans from the active fractions of L. tridentata. One of the compounds, mal.4, was found to be a strong **inhibitor** of HIV transcription, HIV Tat-regulated transactivation and HIV replication.
ABEX Using the Seap bioassay of HIV Tat transactivation and the 2-phase hexane-ethyl acetate-methanol-water solvent system, 2 major components (Gr and Lo) were identified as anti-HIV active principles. The chemical structures of the constituents of Gr

(G1-G4) and Lo (L1-L4) were determined by GC-MS and NMR. After optimization of the isolation conditions, a large-scale isolation with the chloroform-methanol-water system yielded 5 constituents (FB1-FB5). The most predominant anti-HIV compound FB2, denoted Malachi 4:5-6 or mal.4 (heminordihydroguaiaretate), which occurs in 0.23% yield, was separated from its FB1 isomer (0.13% yield). Compound FB4 and the 2 tricyclic lignans (FB3 and FB5) were also isolated in a substantial amount for further testing of their anti-HIV activities. A total of 16 lignans of L. tridentata were identified in this study. Eight of these were structurally new.Although previously described, the lignan 3'-O-methyl **NDGA** (mal.4) is now known for its anti-HIV activity. Mal.4 exerted its **inhibitory** activity by interfering with the binding of Sp1 protein to HIV LTR, thus blocking the proviral transcription, Tat transactivation, and **suppressing viral** replication. (LP)

L37 ANSWER 21 OF 70 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 96310313 MEDLINE
DOCUMENT NUMBER: 96310313
TITLE: Effects of cellular aging on the induction of c-fos by antioxidant **treatments**.
AUTHOR: Keogh B P; Tresini M; Cristofalo V J; Allen R G
CORPORATE SOURCE: Center for Gerontological Research, Medical College of Pennsylvania, Philadelphia 19129, USA.
CONTRACT NUMBER: AG00378 (NIA)
AG00131 (NIA)
AG00523 (NIA)
+
SOURCE: MECHANISMS OF AGEING AND DEVELOPMENT, (1996 Mar 29) 86 (3) 151-60.
Journal code: LMJ. ISSN: 0047-6374.
PUB. COUNTRY: Ireland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY WEEK: 19970104
AB The proto-oncogene c-fos (the cellular homolog of v-fos, Finkel-Biskis-Jenkins (FBJ) murine osteogenic sarcoma **virus**) encodes a major component of the activator protein-1 (AP-1) transcription factor. Serum stimulation as well as oxidizing **treatments** induce transitory increases in c-fos mRNA abundance. The induction of c-fos by serum stimulation is also known to decline during proliferative senesence. In this study, we examined the effects of two classes of antioxidants on the induction of c-fos in early and late passage human fetal lung fibroblasts (WI-38). N-acetyl cysteine (NAC) induces c-fos transcription in both early and late passage cells, while **nordihydroguaiaretic**

acid (NGA) induced c-fos transcription in early passage cells but fails to stimulate it in late passage cells. Since we had previously observed an age-related decline in protein kinase C (PKC) translocation from the cytosol to the membrane, following its activation, and because PKC activation appears to be involved in the NGA induction of c-fos we examined the relative protein abundances of several PKC isoforms in early and late passage cells. Additionally, we examined the protein abundance of several members of the MAP kinase pathway which could play a role in c-fos induction by the PKC-dependent pathway. We were unable to detect PKC-beta or theta in early or late passage cells. Late passage cells contained a slightly greater abundance of PKC alpha, gamma and epsilon than cells at an early passage. No other differences in PKC isoforms or in members of the MAP kinase family were observed in early or late passage cells. These results clearly demonstrate that at least some pathways leading to c-fos induction remain intact in late passage cells. While we were unable to detect any decreases in PKC isoforms or MAP kinase proteins we cannot exclude the possibility that functional decrements accumulate in these proteins during senesence.

L37 ANSWER 22 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96059956 EMBASE
DOCUMENT NUMBER: 1996059956
TITLE: Alterations in reactive oxygen, pH, and calcium in astrocytoma cells during lethal injury.
AUTHOR: Wu Y.; Taylor B.M.; Sun F.F.
CORPORATE SOURCE: Cell Biology/Inflammation Res. Dept., Upjohn Laboratories,Kalamazoo, MI 49001, United States
SOURCE: American Journal of Physiology - Cell Physiology, (1996) 270/1 39-1 (C115-C124).
ISSN: 0363-6143 CODEN: AJPCDD
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
005 General Pathology and Pathological Anatomy
029 Clinical Biochemistry
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Exposure of cultured human astrocytoma cells to iodoacetic acid results in rapid depletion of cellular ATP and cell death. Pathophysiological changes in the injured cells, including formation of reactive oxygen species (ROS), cell viability, glutathione, pH, and cytosolic calcium, were characterized at the cellular level via fluorescence microscopy. After iodoacetic acid treatment, cellular ATP and intracellular glutathione fell sharply to undetectable levels within 2 h. ROS, as detected by the oxidation of dichlorofluorescein, appeared in 20 min and reached a maximum before the loss of membrane integrity. Cells became acidotic within 10 min.

Cytosolic free calcium concentration exhibited a slow increase and then a sharp influx shortly before the rupture of the cell membrane. The addition of lipophilic antioxidants, nordihydroguaiaretic acid or the troloxamine U-78517F, eliminated the accumulation of ROS and delayed the onset of cell death without affecting other parameters observed in the early phase of the injury. We conclude that ROS is formed and may play important roles during lethal cell injury caused by energy depletion.

L37 ANSWER 23 OF 70 TOXLIT
ACCESSION NUMBER: 1996:63015 TOXLIT
DOCUMENT NUMBER: CA-124-167496G
TITLE: Enhancement of introduction of foreign matter into higher eukaryotic cells by co-introduction of anti-apoptosis or anti-inflammatory substances.
AUTHOR: Cotten M; Baker A; Chiocca S
SOURCE: (1995). PCT Int. Appl. PATENT NO. 95 33062 12/07/95 (Boehringer Ingelheim International GmbH).
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Patent
FILE SEGMENT: CA
LANGUAGE: German
OTHER SOURCE: CA 124:167496
ENTRY MONTH: 199605
AB The toxicity problems arising when foreign matter is introduced into higher eukaryotic cells, esp. with transfection with DNA, are obviated by expression in the cell of gene products that block the apoptosis induced by the transfection process and/or by **treating** the cells with anti-inflammatory substances. Preferred anti-apoptosis genes are Bcl-2, adenovirus E1B 19K or an anti-apoptotic gene of the CELO avian adenovirus. The preferred anti-inflammatory substance is adenovirus VA1, which is introduced into the cell in the form of VA1 DNA. These measures help to achieve a long-lasting gene expression. The anti-apoptotic gene of CELO **virus** was cloned and sequenced. The enhancement by the above genes of mammalian cell transfection using transferrin (or streptavidin)-polylysine conjugate/adenovirus transfection complexes was demonstrated. The synergistic effect of anti-inflammatory compds. such as glucocorticoids, ibuprofen, etc. was also shown.

L37 ANSWER 24 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95326741 EMBASE
DOCUMENT NUMBER: 1995326741
TITLE: Characterization of anti-HIV lignans from Larrea tridentata.
AUTHOR: Gnabre J.; Huang R.C.C.; Bates R.B.; Burns J.J.; Calderea S.; Malcomson M.E.; McClure K.J.
CORPORATE SOURCE: Department of Biology, Johns Hopkins University,Baltimore, MD 21218-2685, United States

SOURCE: Tetrahedron, (1995) 51/45 (12203-12210).
ISSN: 0040-4020 CODEN: TETRAB
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Fractions from Larrea tridentata with anti-HIV-1 activity (specifically, **inhibition** of HIV Tat transactivation) were analyzed by GC/MS and found to contain lignans 1a-i and 2a-d. Assay-guided purification by countercurrent chromatography established 1g (mal. 4) to be especially active. Compounds 1b-f,h,i and 2d are new.

L37 ANSWER 25 OF 70 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 96074683 MEDLINE
DOCUMENT NUMBER: 96074683
TITLE: **Inhibition** of human immunodeficiency **virus** type 1 transcription and replication by DNA sequence-selective plant lignans.
AUTHOR: Gnabre J N; Brady J N; Clanton D J; Ito Y; Dittmer J; Bates R B; Huang R C
CORPORATE SOURCE: Department of Biology, Johns Hopkins University, Baltimore, MD 21218, USA.
CONTRACT NUMBER: 5RO132301
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1995 Nov 21) 92 (24) 11239-43.
Journal code: PV3. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199602
AB A plant lignan, 3'-O-methyl **nordihydroguaiaretic** acid (3'-O-methyl **NDGA**, denoted Malachi 4:5-6 or Mal.4; molecular weigth 316), was isolated from Larrea tridentata and found to be able to **inhibit** human immunodeficiency **virus** (HIV) Tat-regulated transactivation in vivo, induce protection of lymphoblastoid CEM-SS cells from HIV (strain IIIB) killing, and **suppress** the replication of five HIV-1 strains (WM, MN, VS, JR-CSF, and IIIB) in mitogen-stimulated peripheral blood mononuclear cells, all in a dose-dependent manner. Mal.4 **inhibits** both basal transcription and Tat-regulated transactivation in vitro. The target of Mal.4 has been localized to nucleotides -87 to -40 of the HIV long terminal repeat. Mal.4 directly and specifically interferes with the binding of Sp1 to Sp1 sites in the HIV long terminal

repeat. By **inhibiting** proviral expression, Mal.4 may be able to interrupt the life cycles of both wild-type and reverse transcriptase or protease mutant **viruses** in HIV-infected patients.

L37 ANSWER 26 OF 70 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1996:67310 BIOSIS
DOCUMENT NUMBER: PREV199698639445
TITLE: Interactions between phytoestrogens and human sex steroid binding protein.
AUTHOR(S): Martin, Marie Elise; Haourigui, Malika; Pelissero, Catherine; Benassayag, Claudine (1); Nunez, Emmanuel A.
CORPORATE SOURCE: (1) U224 INSERM, Fac. Med. Xavier Bichat, 75870 BP 146, Paris France
SOURCE: Life Sciences, (1995) Vol. 58, No. 5, pp. 429-436. ISSN: 0024-3205.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The interactions of human Sex steroid binding protein (SBP), and the lignans (**Nordihydroguaiaretic** acid (**NDGA**) enterolactone (Ent), enterodiol (End)) and isoflavonoid phytoestrogens (Equol (Eq), diazein (Dad), genistein (Gen)) were studied. The phytoestrogens had different dose-dependent **inhibitory** effects on steroid binding by SBP. Their relative efficiencies were : Ent ltoreq **NDGA** = Eq gt Gen for displacing E2 and Eq gt Ent gt **NDGA** gt Gen for displacing T. End and Dad were much less active. Scatchard analysis suggested that **NDGA** had similar non-competitive effects on T and E2 binding by reducing the number of binding sites without changing the association constants. But Eq seemed to **inhibit** E2 binding noncompetitively and T binding competitively. **NDGA** binding to SBP reduced the immunorecognition of SBP by monospecific antiSBP antibodies, suggesting that **NDGA** changed SBP immunoreactivity. Unlike **NDGA**, Eq binding to SBP caused no immunological changes in SBP, indicating qualitative differences in the effects of the lignan and isoflavonoid. Our results indicate that phytoestrogens may modulate the SBP activity and so influence the role of this protein in the delivery of hormonal information to sex steroid-dependent cells.

L37 ANSWER 27 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE 8
ACCESSION NUMBER: 95036795 EMBASE
DOCUMENT NUMBER: 1995036795
TITLE: E1A3Y1 cell-specific toxicity of tea polyphenols and their killing mechanism.
AUTHOR: Mitsui T.; Yamada K.; Yamashita K.; Matsuo N.; Okuda A.; Kimura G.; Sugano M.

CORPORATE SOURCE: Laboratory Food Science/Technology, Faculty of Agriculture, Kyushu University, 6-10-1 Hakozaki,Higashi-ku, Fukuoka 812, Japan
SOURCE: International Journal of Oncology, (1995) 6/2 (377-383).
ISSN: 1019-6439 CODEN: IJONES
COUNTRY: Greece
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB To screen carcinostatic components in foodstuffs, the toxicity of tea polyphenols was compared between rat 3Y1 diploid fibroblasts and a variety of their **virally** transformed cells. Among tea polyphenols tested, epigallocatechin gallate killed 3Y1 cells transformed by E1A gene of human adenovirus type 12; (E1A-3Y1 cells) at a 100 times lower concentration than the parental 3Y1 cells. Epigallocatechin gallate also exerted a strong E1A-3Y1 cell-specific toxicity, while epicatechin and epicatechin gallate did not. When the activity of three antioxidant enzymes was compared between 3Y1 and its transformants, catalase activity was markedly low in the latter, especially in E1A-3Y1 cells, and the substrate of the enzyme, hydrogen peroxide, exerted a toxicity specific to this cell line. Then the **inhibitory** activities of various chemicals on E1A-3Y1 cell-specific toxicity of phospholipids or catechol were examined. Among lipoxygenase **inhibitors**, all of the polyphenolic compounds **inhibited** the toxicity of phospholipids, but not a nonpolyphenolic **inhibitor** (clofibrate). Two phospholipase A2 **inhibitors** (dexamethasone and quinacrine) did not **inhibit** the toxicity. These results indicate that the triphenol structure of the B ring is essential for the E1A-3Y1 cell-specific toxicity of tea polyphenols, and that the decrease in catalase activity is partially responsible for the higher sensitivity of E1A-3Y1 cells against the polyphenols. The **inhibitory** effect of polyphenolic lipoxygenase **inhibitors** is ascribed at least in part to their antioxidant activities.

L37 ANSWER 28 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE 9
ACCESSION NUMBER: 95063785 EMBASE
DOCUMENT NUMBER: 1995063785
TITLE: The non-steroidal anti-inflammatory drug, indomethacin, as an **inhibitor** of HIV replication.
AUTHOR: Bourinbaiar A.S.; Lee-Huang S.

CORPORATE SOURCE: Department of Biochemistry, New York University Medical Center, 550 First Avenue,New York, NY 10016, United States
SOURCE: FEBS Letters, (1995) 360/1 (85-88).
ISSN: 0014-5793 CODEN: FEBLAL
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Indomethacin, a common non-steroidal anti-inflammatory drug (NSAID), has been used to **treat** rheumatoid arthritis. Although indomethacin has also been used as an immunopotentiator and symptomatic NSAID) in AIDS, its effect on HIV replication is unknown. MT-4 lymphocytes were inoculated with HIV in the presence of indomethacin and tested for p24 expression by ELISA. The 50% **inhibition** (IC50,) was 10 .mu.M, corresponding to plasma levels after **administration** of 50 mg oral indomethacin. The **antiviral** effect appears to be specific since no toxicity has been observed at the IC50, dose, and unrelated NSAIDs have not shown the activity at clinical doses. Indomethacin may, thus, represent a new class of anti-HIV drug.

ACCESSION NUMBER: 1994-200294 [24] WPIDS
DOC. NO. CPI: C94-091594
TITLE: Identifying cpds. with neuro protective activity - against organisms causing e.g. encephalitis by **inhibiting** release of platelet activation factor and arachidonate metabolites.
DERWENT CLASS: B04 D16
INVENTOR(S): BERNTON, E W; GENDELMAN, H; JETT, M
PATENT ASSIGNEE(S): (USSA) US DEPT OF ARMY
COUNTRY COUNT: 19
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9412667	A1	940609	(9424)*	EN	40

RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: CA JP US

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9412667	A1	WO 93-US11542	931129

Searcher : Shears 308-4994

PRIORITY APPLN. INFO: US 92-982656 921127; US 93-61970 930902
AN 1994-200294 [24] WPIDS
AB WO 9412667 A UPAB: 19940803
Screening cpds. screened for neuroprotective activity comprises (1) infecting cultured monocytes or leucocytes with an organism known to cause neuronal damage; (2) adding astrocytes and then test cpds. to the infected cultures; (3) incubating to allow prodn. of TNF (tumour necrosis factor) alpha; (4) withdrawing aliquots of supernatant and adding to neuron-contg. cultures; (5) incubating then examining cells for neurotoxic or neurocytopathic effects.

Also claimed are (1) supernatant in a culture of neurons, of a culture contg. infected monocytes/lymphocytes and astrocytes; (2) compsns. contg. neuroprotective amts. of 11-nor-delta8 -tetrahydrocannabinol-9-carboxylic acid (I) or (for delivery through the mucosa) **NDGA** (**nordihydroguaiaretic** acid).

USE - The method detects cpds. which **inhibit** release of, or antagonise, arachidonate metabolites and platelet activation factor (PAF) which cause neuronal damage (encephalopathy and encephalitis) following **viral** (esp. HIV), parasitic or bacterial infection of the CNS. The cpds. may also include replication and release of infectious **virus** and, for HIV **treatment**, can be combined with other drugs for control of retroviral infections.
Dwg.0/0

L37 ANSWER 30 OF 70 SCISEARCH COPYRIGHT 1999 ISI (R)
ACCESSION NUMBER: 94:152416 SCISEARCH
THE GENUINE ARTICLE: NB409
TITLE: PREFERENTIAL **INHIBITION** OF PLATELET-DERIVED GROWTH FACTOR-STIMULATED DNA-SYNTHESIS AND PROTEIN-TYROSINE PHOSPHORYLATION BY **NORDIHYDROGUAIARETIC** ACID
AUTHOR: DOMIN J; HIGGINS T; ROZENGURT E (Reprint)
CORPORATE SOURCE: IMPERIAL CANC RES FUND, 44 LINCOLNS FIELDS, LONDON WC2A 3PX, ENGLAND (Reprint); IMPERIAL CANC RES FUND, LONDON WC2A 3PX, ENGLAND
COUNTRY OF AUTHOR: ENGLAND
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (18 MAR 1994) Vol. 269, No. 11, pp. 8260-8267.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 56
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB **Nordihydroguaiaretic** acid (**NDGA**), a reportedly specific lipoxygenase **inhibitor**, was found to

selectively **inhibit** platelet-derived growth factor (PDGF)-stimulated DNA synthesis in Swiss 3T3 cells. Maximal **inhibition** of PDGF-induced [H-3]thymidine incorporation (96%) was observed using 4 mu M **NDGA** (IC50 = 1.5 mu M). No effect of **NDGA** was observed upon DNA synthesis stimulated with either fetal bovine serum, bombesin, or epidermal growth factor (EGF) in the presence of insulin, or with the potent mitogen Pasteurella multocida toxin. The selective **inhibition** of PDGF-stimulated DNA synthesis by **NDGA** was also observed in diploid murine cells, rat, and human fibroblasts. Furthermore, 4 mu M **NDGA** also **inhibited** PDGF-stimulated anchorage-independent colony growth of rat-1 cells by 76%. Using Swiss 3T3 cells, we found that PDGF-stimulated arachidonic acid mobilization and prostaglandin E(2) production was abolished by **NDGA** in a dose-dependent manner. **Inhibition** of PDGF-stimulated arachidonic acid mobilization by **NDGA** could not, however, explain its potent **inhibitory** effect upon PDGF-stimulated DNA synthesis.

Our results showed that **NDGA** also selectively **inhibited** PDGF receptor tyrosine phosphorylation in a dose-dependent manner in intact cells. Protein tyrosine phosphorylation stimulated by EGF or bombesin was not altered by **NDGA treatment**. Crucially, **NDGA** **inhibited** in vitro the tyrosine kinase activity of anti-phosphotyrosine and anti-PDGF receptor immunoprecipitates prepared from cultures stimulated with PDGF. This **inhibition** of receptor tyrosine phosphorylation in a cell-free system confirmed that **NDGA** acts directly at the level of the PDGF receptor tyrosine kinase domain. These results suggest that the potent and selective **inhibitory** effect of **NDGA** on PDGF-stimulated DNA synthesis results from its **inhibitory** action on tyrosine phosphorylation.

L37 ANSWER 31 OF 70 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 94333933 MEDLINE
DOCUMENT NUMBER: 94333933
TITLE: The immortalized astroglial cell line RC7 is a new model system for the study of nerve growth factor (NGF) regulation: stimulation by interleukin-1 beta and transforming growth factor-beta 1 is additive and affected differently by dibutyryl cyclic AMP.
AUTHOR: Hahn M; Lorez H; Fischer G
CORPORATE SOURCE: Pharma Division, F. Hoffmann-La Roche Ltd., Basel, Switzerland.
SOURCE: GLIA, (1994 Apr) 10 (4) 286-95.
Journal code: GLI. ISSN: 0894-1491.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
AB Nerve growth factor (NGF) synthesis was studied with an astroglial cell line derived from rat cerebellar astrocytes by transfection with a simian **virus** 40 T containing retroviral vector. As in primary astrocytes, NGF synthesis/secretion could be stimulated dose-dependently with interleukin-1 beta (IL-1 beta) and transforming growth factor-beta 1 (TGF-beta 1). We therefore have used this cell line as a model system to analyze putative intracellular signalling pathways underlying the effects of these factors. Protein kinase C **inhibitors** (calphostin and Ro 31-8830) as well as a lipoxygenase **inhibitor** (**nordihydroguaiaretic** acid) did not affect stimulation of NGF synthesis/secretion by IL-1 beta or TGF-beta 1. However, dibutyryl cyclic AMP partly **inhibited** the stimulation by TGF-beta 1 but did not affect that evoked by IL-1 beta. This finding, together with the fact that IL-1 beta and TGF-beta 1 stimulate NGF production/secretion in an additive manner, indicates that different intracellular signalling pathways are involved in the mediation of IL-1 beta and TGF-beta 1 induced NGF production/secretion.

L37 ANSWER 32 OF 70 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 94304215 MEDLINE
DOCUMENT NUMBER: 94304215
TITLE: Expression of porcine leukocyte 12-lipoxygenase in a baculovirus/insect cell system and its characterization.
AUTHOR: Reddy R G; Yoshimoto T; Yamamoto S; Funk C D; Marnett L J
CORPORATE SOURCE: A.B. Hancock, Jr., Memorial Laboratory for Cancer Research, Department of Biochemistry, Vanderbilt University School of Medicine, Nashville, Tennessee 37232-0146.
CONTRACT NUMBER: CA47479 (NCI)
ES00267 (NIEHS)
SOURCE: ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, (1994 Jul) 312 (1) 219-26.
Journal code: 6SK. ISSN: 0003-9861.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199410
AB Arachidonate 12-lipoxygenase (12-LO) from porcine leukocytes was expressed in insect cells using a baculovirus expression vector. The recombinant 12-LO was expressed as an N-terminal fusion protein with a 31-amino acid polypeptide carrying a six-histidine tag and an enterokinase cleavage site. Maximal intracellular enzyme activity and protein levels were observed 48 h after infection of Spodoptera

frugiperda cells with the recombinant **virus**. Cells were lysed and the recombinant protein was purified in a single step by Ni2+-nitrilotriacetate column chromatography. The purified enzyme migrated as a single band on sodium dodecyl sulfate-polyacryl-amide gel electrophoresis. Recombinant enzyme catalyzed the formation of 12-hydroperoxy-5,8,10,14-eicosatetranoic acid and a small amount of 15-hydroperoxy-5,8,11,13-eicosatetraenoic acid. Chiral-phase HPLC analysis indicated that the 12-(S) enantiomer was the predominant product. The purified recombinant 12-lipoxygenase oxygenated linoleic acid to about 19% of the extent of oxygenation of arachidonic acid. **Nordihydroguaiaretic** acid and 5,8,11,14-eicosatetraynoic acid **inhibited** the recombinant enzyme with IC50's of 2.2 and 0.06 micM, respectively. Expression of cloned porcine leukocyte 12-LO in S. frugiperda cells and purification by Ni2+-nitrilotriacetate chromatography provides a straightforward method for isolation of milligram quantities of this form of 12-LO.

L37 ANSWER 33 OF 70 AIDSLINE
ACCESSION NUMBER: 1995:12992 AIDSLINE
DOCUMENT NUMBER: AIDS-95921601
TITLE: **Inhibition** of arachidonate metabolism alters HIV-1 replication and cytopathicity in monocytes.
AUTHOR: Genis P; Jett M; Franson R; Gendleman H E; Bernton E
CORPORATE SOURCE: Univ. of Nebraska Medical Center, Omaha, NE.
SOURCE: Natl Conf Hum Retroviruses Relat Infect (1st), (1993). pp. 161.
PUB. COUNTRY: United States
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: AIDS
LANGUAGE: English
ENTRY MONTH: 199512

AB The interactions between HIV-1 infected monocytes and astroglia result in eicosanoid production that modulates cytokine and neurotoxic activities from **virus**-infected monocytes. (Genis, 1992, J. Exp. Med. 176:1703). To investigate the role of eicosanoids in HIV-1 neuropathogenesis, we determined whether arachidonate metabolite **inhibitors** altered HIV replication. Monocytes purified by centrifugal elutriation were inoculated with HIV-1 ADA at an MOI=1. During the course of infection cells were **treated** with either **nordihydroguaiaretic** acid (**NDGA**), a non-specific lipoxygenase **inhibitor**, THC-7-oic acid (THC7), a PAF antagonist, indomethacin, a cyclooxygenase **inhibitor**, or dexamethasone (DEX) or PX-52, both **inhibitors** of phospholipase A2, at concentrations from 2-100 micromolar. RT activity and syncytia were monitored over a 14 day period. Monocyte viability was confirmed by NBT dye reduction. DEX and **NDGA**

reduced greater than 3-fold HIV replication and **virus** -induced cytopathicity. Interestingly, indomethacin increased both Rt activity and cytopathicity. THC7 and PX52 had modest effects on HIV production. These data suggest that arachidonate metabolites regulate HIV replication and cytopathicity in monocytes. **Inhibitors** of these pathways could effect HIV infection in brain macrophages.

L37 ANSWER 34 OF 70 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1993:431582 BIOSIS
DOCUMENT NUMBER: PREV199396086207
TITLE: Effects of alpha-2- and beta-adrenergic agonism on glucagon secretion from perfused pancreata of normal and streptozocin-induced diabetic rats.
AUTHOR(S): Hirose, Hiroshi (1); Maruyama, Hiroshi; Ito, Katsuhiko; Kido, Koichi; Koyama, Kazunori; Saruta, Takao
CORPORATE SOURCE: (1) Dep. Internal Med., Keio Univ. Sch. Med., 35 Shinanomachi, Shinjuku-ku, Tokyo 160 Japan
SOURCE: Metabolism Clinical and Experimental, (1993) Vol. 42, No. 8, pp. 1072-1076.
ISSN: 0026-0495.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Insulin secretion is known to be inhibited by alpha-2-adrenergic agonism and stimulated by beta-adrenergic agonism in both experimental animals and humans. In contrast, adrenergic regulation of glucagon secretion remains controversial. This study was designed to determine the effects of alpha-2- and beta-adrenergic agonism on islet alpha cells, using isolated perfused pancreata of normal and streptozocin-induced diabetic (STZ-D) rats. The alpha-2-adrenoceptor agonist clonidine at a concentration of 10-7 mol/L significantly stimulated glucagon secretion as compared with basal levels in both normal (1,286 +- 90 v 417 +- 53 ng/L, P lt .01) and STZ-D rats (551 +- 86 v 130 +- 19 ng/L, P lt .01). Also, the beta-adrenoceptor agonist isoproterenol at a concentration of 10-7 mol/L significantly stimulated glucagon secretion as compared with basal levels in both normal (751 +- 130 v 347 +- 41 ng/L, P lt .05) and STZ-D rats (182 +- 22 v 92 +- 20 ng/L, P lt .01). Furthermore, these alpha-2- and beta-agonistic effects were almost completely inhibited in the presence of the alpha-2-adrenoceptor antagonist yohimbine and the beta-adrenoceptor antagonist propranolol at a concentration of 10-6 mol/L, respectively. Insulin secretion was markedly reduced in STZ-D rats. These results suggest that even in a severely diabetic state, not only beta- but also alpha-2-adrenergic agonism stimulates glucagon secretion from rat pancreatic alpha cells.

L37 ANSWER 35 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE 12

ACCESSION NUMBER: 93179288 EMBASE
DOCUMENT NUMBER: 1993179288
TITLE: Poly I:C-induced **antiviral** and cytotoxic activities are mediated by different mechanisms.
AUTHOR: Pyo S.; Gangemi J.D.; Ghaffar A.; Mayer E.P.
CORPORATE SOURCE: Dept. of Microbiology/Immunology, University of South Carolina, School of Medicine,Columbia, SC 29208, United States
SOURCE: International Journal of Immunopharmacology, (1993) 15/4 (477-486).
ISSN: 0192-0561 CODEN: IJIMDS
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
016 Cancer
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Macrophages play an important role in host defenses against tumors and **virus** infections by killing tumor or **virus** infected cells (extrinsic cytotoxicity) and by limiting **virus** replication within themselves (intrinsic **antiviral** activity). Since common macrophage products may be involved in both extrinsic cytotoxicity and intrinsic **antiviral** activity, we decided to investigate the mechanisms by which Poly I:C-activated macrophages resist infection with HSV-1 and **inhibit** the growth of tumor cells. The ability of macrophages to resist infection with HSV-1 or to **inhibit** growth of tumor cells was assessed following **treatment** with Poly I:C in the presence of antibodies to various cytokines or in the presence of **inhibitors**/scavengers of toxic macrophage products. Only antibodies to IFN-.beta. were able to abrogate the protective effects of Poly I:C in macrophages infected with HSV-1, suggesting that the **antiviral** activity induced by this immunomodulator was mediated by the production of IFN-.beta., which acted in an autocrine manner. In contrast, anti-TNF-.alpha., anti-IFN-.alpha./.beta., anti-IFN-.beta. antibodies and **inhibitors** of nitric oxide and C1q production were all able to partially abrogate Poly I:C-induced cytostatic activity, suggesting that multiple mechanisms are involved in macrophage cytostasis. Our results indicate the Poly I:C-induced intrinsic **antiviral** and extrinsic cytotoxic activities are mediated by different mechanisms.

L37 ANSWER 36 OF 70 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1993:431581 BIOSIS

DOCUMENT NUMBER: PREV199396086206
TITLE: Protection of islet cells from inflammatory cell death in vitro.
AUTHOR(S): Burkart, V. (1); Kolb, H.
CORPORATE SOURCE: (1) Diabetes Res. Inst., Auf'm Hennekamp 65, D-40225 Duesseldorf Germany
SOURCE: Clinical and Experimental Immunology, (1993) Vol. 93, No. 2, pp. 273-278.
ISSN: 0009-9104.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Islet cells cocultured with activated macrophages are lysed within 15 h in vitro. We showed previously that nitric oxide generated by macrophages is a major mediator of islet cell death. We have now probed several pathways to interfere with the chain of events leading to islet cell death. Scavenging of extracellular oxygen radicals by superoxide dismutase and catalase did not improve islet cell survival. Scavenging of extra- and intracellular oxygen radicals by two potent substances, citiolone and dimethyl-thiourea, also did not reduce islet cell lysis, while a lipid-soluble scavenger, probucol, provided partial protection. These findings argue against a synergistic action of nitric oxide and oxygen radicals in islet cell toxicity. The inhibition of poly(ADP-ribose)polymerase by 3-aminobenzamide significantly improved islet cell survival. Selective inhibitors of cyclooxygenase, such as indomethacin or acetylsalicylic acid, did not improve islet cell survival. Full protection was seen in the presence of NDGA, an inhibitor of lipoxygenase, and partial suppression was caused by BW755c, an inhibitor of both lipoxygenase and cyclooxygenase. We conclude that inflammatory islet cell death caused by activated macrophages involves the activation of arachidonic acid metabolism and of poly(ADP-ribose)polymerase, but that scavenging of oxygen free radicals provides little protection from lysis.

L37 ANSWER 37 OF 70 MEDLINE
ACCESSION NUMBER: 93285336 MEDLINE
DOCUMENT NUMBER: 93285336
TITLE: Correlation between phospholipase A2 activity and intra-Golgi protein transport reconstituted in a cell-free system.
AUTHOR: Tagaya M; Henomatsu N; Yoshimori T; Yamamoto A; Tashiro Y; Fukui T
CORPORATE SOURCE: Institute of Scientific and Industrial Research, Osaka University, Japan.
SOURCE: FEBS LETTERS, (1993 Jun 14) 324 (2) 201-4.
Journal code: EUH. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199309
AB A wide variety of phospholipase A2 **inhibitors** blocks intra-Golgi protein transport reconstituted in a cell-free system. Phospholipase A2 activity detectable under the protein transport assay conditions is actually **inhibited** by the **inhibitors**. There is a good correlation between the **inhibition** of protein transport and that of phospholipase A2 activity. Prolactin secretion from GH3 cells is also blocked by a membrane-permeable phospholipase A2 **inhibitor**, suggesting the physiological relevance to **inhibition** of protein transport in vitro by phospholipase A2 **inhibitors**.

L37 ANSWER 38 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93084468 EMBASE
DOCUMENT NUMBER: 1993084468
TITLE: 1992 new drug approvals.
SOURCE: Hospital Formulary, (1993) 28/2 (125-127).
ISSN: 0098-6909 CODEN: HOFOD
COUNTRY: United States
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L37 ANSWER 39 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93168249 EMBASE
DOCUMENT NUMBER: 1993168249
TITLE: Squamous cell carcinoma of the skin: Will heightened awareness of risk factors slow its increase?.
AUTHOR: Hacker S.M.; Flowers F.P.
CORPORATE SOURCE: Division of Dermatology, Florida University Coll. of Medicine, PO Box 100277,Gainesville, FL 32610-0277, United States
SOURCE: Postgraduate Medicine, (1993) 93/8 (115-126).
ISSN: 0032-5481 CODEN: POMDAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 013 Dermatology and Venereology
016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Although squamous cell carcinoma of the skin is still less common than basal cell carcinoma, its incidence is increasing at an alarming rate. Cumulative sun exposure is a major risk factor, and deterioration of the ozone layer combined with life-style choices that promote time in the sun may account for part of the increased

incidence. Other risk factors for squamous cell carcinoma include exposure to ionizing radiation, arsenic, or industrial chemicals; **viral** infection; preexisting burns and scars; and immunosuppression. Actinic keratosis is considered a precancerous lesion that should be watched closely. **Treatment** methods for squamous cell carcinoma vary depending on the size and location of the lesion. Knowledge of high-risk locations and appropriate **treatment** choices ensures proper care and decreases the likelihood of metastasis.

L37 ANSWER 40 OF 70 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 93287009 MEDLINE
DOCUMENT NUMBER: 93287009
TITLE: Immunomodulation of cellular cytotoxicity to **herpes** simplex **virus** infection in pregnancy by **inhibition** of eicosanoid metabolism.
AUTHOR: Feinberg B B; Tan N S; Donovan P K; Loftin K C; Gonik B
CORPORATE SOURCE: Department of Obstetrics, Gynecology and Reproductive Sciences, University of Texas Medical School, Houston.
SOURCE: JOURNAL OF REPRODUCTIVE IMMUNOLOGY, (1993 Mar) 23 (2) 109-18.
Journal code: JWS. ISSN: 0165-0378.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199309

AB In an effort to evaluate the relationships among pregnancy, cellular cytotoxicity and **herpes** simplex **virus** (**HSV**) infection, we conducted a series of experiments investigating: (1) the maternal cellular cytotoxic response to **HSV** infection as compared with non-pregnant hosts, (2) the influence of both cyclooxygenase and lipoxygenase products on cytotoxicity by selective **inhibition** of their metabolic pathways, and (3) the potential pregnancy-related differences in immune response to selective **inhibition** of eicosanoid metabolism. Indomethacin was used for cyclooxygenase blockade and **nordihydroguaiaretic** acid was used to evaluate lipoxygenase **inhibition**. In the non-infected animals no differences in cytotoxicity were observed between pregnant (1.5% +/- 0.7%) and non-pregnant (4.6% +/- 2.0%) groups. **HSV** infection increased cytotoxicity equally in both groups (pregnant: 10.6% +/- 2.0% vs. non-pregnant: 14.2% +/- 3.4%). Indomethacin did not significantly alter cytotoxicity in either the pregnant or the non-pregnant groups compared with controls (12.8% +/- 1.8% vs. 10.6% +/- 2.0% and 14.3% +/- 3.9% vs. 14.2% +/- 3.4%, respectively). In

contrast, **NDGA** elicited a significant reduction in the cytotoxic response in both pregnant and non-pregnant hosts (6.2% +/- 1.1% vs. 10.6% +/- 2.0% and 5.7% +/- 1.1% vs. 14.2% +/- 3.4%, respectively). From our study we conclude that: (1) cytotoxicity is maintained at low levels in the absence of **HSV** infection, (2) **HSV** infection induces a significant augmentation in host cellular cytotoxicity, (3) pregnant and non-pregnant cytotoxic responses to **HSV** infection appear comparable, (4) indomethacin does not augment in vitro cytotoxicity to **HSV** infection and (5) **NDGA suppresses** cytotoxicity, providing evidence that lipoxygenase metabolites are essential to cytotoxic cell function.

L37 ANSWER 41 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93120951 EMBASE
DOCUMENT NUMBER: 1993120951
TITLE: 1992 drug approvals: The year in review.
AUTHOR: Estrada J.
SOURCE: Drug Therapy, (1993) 23/3 (55-58+63).
ISSN: 0001-7094 CODEN: DRTHE2
COUNTRY: United States
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Twenty-six new molecular entities were approved by the FDA in 1992. Several of them were the first in new classes of drugs to reach the market. Other firsts included the first joint review of a drug by the FDA and the Canadian Health Protection Branch and the availability of a once-daily NSAID and a once-daily quinolone antibiotic. Consumers are keeping their eyes on finasteride, the first nonsurgical **treatment** for benign prostatic hyperplasia, and sumatriptan, a promising new migraine remedy. Several drugs of interest to AIDS patients were also approved. Following is a brief summary of information about each new entity approved in 1992.

L37 ANSWER 42 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93058339 EMBASE
DOCUMENT NUMBER: 1993058339
TITLE: P and T update: New approvals and dosage forms.
SOURCE: Hospital Formulary, (1993) 28/1 (7-8+13).
ISSN: 0098-6909 CODEN: HOFOD
COUNTRY: United States
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index

038 Adverse Reactions Titles
LANGUAGE: English

L37 ANSWER 43 OF 70 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1993:74237 BIOSIS
DOCUMENT NUMBER: PREV199395038737
TITLE: Redox status of cells influences constitutive or induced NF-kappa-B translocation and HIV long terminal repeat activity in human T and monocytic cell lines.
AUTHOR(S): Israel, Nicole (1); Gougerot-Pocidalo, Marie-Anne; Aillet, Fabienne; Virelizier, Jean-Louis
CORPORATE SOURCE: (1) Unite d'Immunologie Virale, Inst. Pasteur, 75724 Paris Cedex 15 France
SOURCE: Journal of Immunology, (1992) Vol. 149, No. 10, pp. 3386-3393.
ISSN: 0022-1767.
DOCUMENT TYPE: Article
LANGUAGE: English

AB We have tested the hypothesis that cellular activation events occurred in T lymphocytes and monocyte and mediated through translocation of the transcription factor NF-kappa-B are dependent upon the constitutive redox status of these cells. We used phenolic, lipid-soluble, chain-breaking antioxidants butylated hydroxyanisole (BHA), nordihydroquairetic acid, or alpha-tocopherol (vitamin E) to show that peroxyl radical scavenging in unstimulated and PMA- or TNF-stimulated cell blocks the functions depending on NF-kappa-B activation. BHA was found to **suppress** not only PMA- or TNF-induced, but also constitutive. HIV-enhancer activity concomitant to an **inhibition** of NF-kappa-B binding activity in both lymphoblastoid T (J.Jhan) and monocytic (U937) cell lines. This was also true for KBF (p50 homodimer) binding activity in U937 cells. Secretion of TNF, the product of another NF-kappa-B dependent gene, was abolished by BHA in PMA-stimulated U937 cells. The anti-oxidative effect of BHA was accompanied by an increase in thiol, but not glutathione, content in stimulated and unstimulated T cells, whereas TNF stimulation itself barely modified the cellular thiol level. Oxidative stress obtained by the addition of H-2O-2 to the culture medium of J.Jhan or U937 cells could not by itself induce NF-kappa-B activation. These observations suggest that TNF and PMA did not lead to NF-kappa-B activation through induction of changes in the cell redox status. Rather, TNF and PMA can exert their effect only if cells are in an appropriate redox status, because prior modification toward reduction with BHA **treatment prevents** this activation. It appears that a basal redox equilibrium tending toward oxidation is a prerequisite for full activation of transduction pathways regulating the activity of NF-kappa-B-dependent genes.

L37 ANSWER 44 OF 70 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1992:261701 BIOSIS
DOCUMENT NUMBER: BA93:138026
TITLE: DIETHYLDITHIOCARBAMATE DITHIOCARB SODIUM EFFECT ON ARACHIDONIC ACID METABOLISM IN HUMAN MONONUCLEAR CELLS GLUTATHIONE PEROXIDASE-LIKE ACTIVITY.
AUTHOR(S): HOSNI M; MESKINI N; PRIGENT A-F; ANKER G; JOULAIN C; EL HABIB R; LAGARDE M
CORPORATE SOURCE: INSERM UNITE 205, LABORATOIRE CHIMIE BIOLOGIQUE, BAT. 406, INSTITUT NATIONAL SCIENCES APPLIQUEES DE LYON, 20 AVENUE A. EINSTEIN, 69621 VILLEURBANNE, FR.
SOURCE: BIOCHEM PHARMACOL, (1992) 43 (6), 1319-1329.
CODEN: BCPCA6. ISSN: 0006-2952.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Diethyldithiocarbamate (DTC), a thiol delivery agent, has been shown to significantly reduce the frequency of primary opportunistic infections in HIV-infected patients. This **therapeutic** effect has been related to the capacity of DTC to reverse the deleterious effects of the oxidative stress occuring in HIV infection. The influence of DTC on the oxygenated metabolism of arachidonic acid (AA) was investigated in mitogen-stimulated human peripheral blood mononuclear cells (PBMC0. Upon incubation with PBMC previously labelled with [3H]AA, Concanavalin A (Con A) markedly increased cyclooxygenase and lipoxygenase activities, within 30 min, as judged by thromboxane B2 (TxB2) and hydroxyeicosatetraenoic acid (HETE) production. Con A activation of [3H]AA platelets also increased 12-HETE production but did not induce any TxB2 synthesis. Micromolar concentrations of DTC, added simultaneously with the mitogen, significantly enhanced the synthesis of HETEs above the Con A-induced level while TxB2-induced synthesis was **inhibited** but only at DTC concentrations higher than 50 .mu.M. In the presence of **nordihydroguaiaretic** acid, a lipoxygenase **inhibitor**, which **inhibited** the Con A-induced synthesis of HETEs by 78%, DTC no longer stimulated HETE production above the Con A-induced level. Reverse phase HPLC analysis showed that Con A increased the PBMC production of 5-, 12- and 15-HETEs. In the presence of 5 .mu.M DTC, 5-HETE production was entirely **suppressed** whereas the 15-HETE level was markedly enhanced, 12-HETE produciton by the contaminating platelets remained unchanged. In vitro experiments indicated that DTC alone did not significantly influence 15-hydroperoxyeicosatetraenoic (15-HPETE) production by the soybean 15-lipoxygenase but, in the presence of added reduced glutathione, DTC markedly reduced 15-HPETE into 15-HETE. In addition, DTC was able to substitute for cellular extract in the glutathione peroxidase (GPx) assay system. Taken together, these results indicate that DTC, through its "GPx-like" activity is able to modify the lipoxygenase cascade. Its ability to selectively reduce 15-HPHETE known to stimulate immunosuppressive

T-cells might help to explain its positive regulatory effect upon the immune system.

L37 ANSWER 45 OF 70 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 92405734 MEDLINE
DOCUMENT NUMBER: 92405734
TITLE: Stimulation of receptor-coupled phospholipase A2 by interferon-gamma.
AUTHOR: Ponzoni M; Montaldo P G; Cornaglia-Ferraris P
CORPORATE SOURCE: Pediatric Oncology Research Laboratory, G. Gaslini Children's Hospital, Genoa, Italy.
SOURCE: FEBS LETTERS, (1992 Sep 21) 310 (1) 17-21.
Journal code: EUH. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199212

AB The biomolecular mechanisms that mediate signal transduction by type II (gamma) interferon (IFN) are poorly understood. IFN-gamma is a potent growth **inhibitory** cytokine also endowed with **antiviral**, immunomodulatory, and differentiating activities on various cell targets, including neural cells. IFN-gamma induced a rapid and transient activation of phospholipase A2 in LAN-5, a human neuroblastoma cell line. A consequence of phospholipase A2 activation was the release of arachidonic acid and the generation of lysophospholipids from membrane phospholipids. **Treatment** of pre-labeled LAN-5 cells with a receptor-saturating concentration of IFN-gamma led to a time-dependent release of [3H]arachidonic acid into the culture media and generation of [32P]lysophosphatidylcholine. Pretreatment of cultures with the phospholipase A2 **inhibitor**, bromophenacyl bromide, markedly **inhibited** both [3H]arachidonic acid release and lysophosphatidylcholine production induced by IFN-gamma **treatment**. Pretreatment of LAN-5 cells with **nordihydroguaiaretic** acid, a lipoxygenase **inhibitor**, or with indomethacin, a cyclooxygenase **inhibitor**, amplified the release of [3H]arachidonic acid and production of lysophosphatidylcholine induced by non-saturating concentrations of IFN-gamma. In parallel, and with the same time-dependent effect, a significant decrease in phosphatidylcholine labeling was observed in IFN-gamma-**treated** cells, further indicating that a potential signal transduction mechanism of IFN-gamma is the hydrolysis of membrane phosphatidylcholine by phospholipase A2.

L37 ANSWER 46 OF 70 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 92-46813 DRUGU M P E
TITLE: Biological Activities and Mechanisms of Action of PGJ2 and Related Compounds: an Update.

Searcher : Shears 308-4994

AUTHOR: Fukushima M
LOCATION: Nagoya, Japan
SOURCE: Prostaglandins Leukotrienes Essent.Fatty Acids (47, No. 1, 1-12, 1992) 3 Fig. 124 Ref.
CODEN: PLEAEU ISSN: 0952-3278
AVAIL. OF DOC.: Department of Internal Medicine, Aiichi Cancer Center, Chikusa-ku, Nagoya 464, Japan.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 92-46813 DRUGU M P E
AB Recent advances in the biological activity and mechanism of action of PGJ2 and related compounds is reviewed. Effects on cell division, binding to fatty acid binding proteins, involvement in heat shock, **antiviral** activity, stimulation of osteogenesis, inflammatory activity, antiproliferative activity and in-vivo antitumor activity in animals are discussed. Further studies may discern the common vulnerability of malignant cells and may provide a new chemotherapeutic strategy.

ABEX The chemistry of alkylidene cyclopentenone PG is detailed (with reference to delta-7-PGA1, clavulone-1, punaglandin-3, TEI-3313). The natural occurrence of delta-12-PGJ2 is discussed. Cyclopentenone and alkylidene cyclopentenone PG disturb membrane integrated systems including precursor uptake, adenylate cyclase, Ca-stimulated ATPase and calmodulin-dependent guanylate cyclase. Gamma-glutamyl-cysteine synthetase is induced by cyclopentenone PG. The involvement of cyclopentenone PG in heat shock is detailed; the cellular response to cyclopentenone PG is similar to that induced by arsenite. The **antiviral** activity of PG including PGA1 and 16,16-dimethyl-PGQ2-methylester is detailed. Delta-12-PGJ2 and TEI-3313 have activity similar to L-alpha-25-dihydroxyvitamin D3 in stimulating osteogenesis. The inflammatory effects of PGJ2 are compared with 9alpha,11beta-PGF2, BN24SC, and PGD2. Antiproliferative effects of PG (e.g. delta-7-PGA1, delta-12-PGJ2, OP-41483, 11-HETE, misoprostol) have been demonstrated in various cells (endometrial carcinoma, ML-1, HL-60, U-937, ovarian carcinoma, human glioma) effects of ketoprofen, **NDGA**, AA-863, U-60257 (piriprost), AA-861 (docebenone), quercetin, 5-HETE, cisplatin, doxorubicin, and l-phenylalanine mustard are also detailed. I.p. delta-12-PGJ2 **suppresses** the growth of human colon cancer in mice. Delta-7-PGA1 and TEI-0303 **suppress** VX-2 tumor growth in rabbits. Future perspectives are detailed. Evaluation of an adjuvant effect of delta-7-PGA1 to cisplatin and synergistic effects of delta-12-PGJ2 and tumor necrosis factor may help develop a new concept of chemotherapy. (E35/LJ)

ACCESSION NUMBER: 91082447 MEDLINE
DOCUMENT NUMBER: 91082447
TITLE: **Inhibitors** of the lipoxygenase pathway specifically block orthopoxvirus replication.
AUTHOR: Palumbo G J; Buller R M
CORPORATE SOURCE: Laboratory of Viral Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892.
SOURCE: VIROLOGY, (1991 Jan) 180 (1) 457-63.
Journal code: XEA. ISSN: 0042-6822.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199104

AB **Inhibitors** of arachidonic acid metabolism, 5,8,11,14-eicosatetraynoic acid (ETYA), BW755c, and **nordihydroguaiaretic** acid were found to specifically interfere with the replication of cowpox **virus** (an orthopoxvirus) both in vivo and in vitro. Further studies in vitro showed that the drugs ETYA and BW755c were effective in **inhibiting** the replication of two additional orthopoxviruses, ectromelia and vaccinia **viruses**, but not human parainfluenza **virus**-3. In ETYA-**treated** and cowpox **virus**-infected cells, early and late gene expression were near normal levels, whereas the assembly of **virus**-specific membranes was severely reduced. These results are compatible with a model of orthopoxvirus replication that has an obligate requirement for arachidonic acid or one of its metabolic forms, possibly in the assembly of **virus**-specific membranes.

L37 ANSWER 48 OF 70 PROMT COPYRIGHT 1999 IAC

ACCESSION NUMBER: 91:196515 PROMT
TITLE: IN THE PUBLIC EYE: Media Exaggerates Benefits of Laser **Therapy**, Some Contend
SOURCE: Dermatology Times, (Apr 1991) pp. 36.
ISSN: 0196-6197.
LANGUAGE: English
WORD COUNT: 893
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB This monthly column contains abstracts of articles from consumer publications on topics relevant to dermatology. By being alerted to articles appearing in the lay press, you may be better prepared to answer questions, correct erroneous or misinterpreted information, offer patients easy-to-read discussions of dermatology and skin care, and become attuned to how the media cover dermatologic issues. Health (February 1991)

Searcher : Shears 308-4994

"The benefits of lasers are being hyped by overly optimistic news reports, a public enthralled with the instruments' novelty, and competitive physicians, hospitals, and laser companies eager to cash in on the devices' high-tech image." This atmosphere lends a premature air of validity to some laser **treatments**, some contend. The primary example cited was a case of permanent dot scarring as a result of spider vein laser **treatment**.
Many doctors believe that lasers should only be used when clinical trials have demonstrated a significant advantage over traditional techniques. Consistently successful laser **treatment** of spider veins, for instance, has not been demonstrated, but Q-switched ruby laser tattoo removal has been clearly established.
The American Society of Plastic and Reconstructive Surgeons (ASPRS) ... issued a statement warning the public about "potential risks and drawbacks of certain experimental laser procedures."
Mademoiselle (March 1991)
Stress can trigger an imbalance in the endocrine system and weaken the immune system, leading to various skin disorders, such as canker sores, cold sores, and acne. Cold sores are highly contagious **viral** infections.
By Tom Celebrezze

L37 ANSWER 49 OF 70 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1990-336689 [45] WPIDS
DOC. NO. CPI: C90-146074
TITLE: Use of arachidonic acid or its analogue - for **treatment** of cytokine mediated diseases e.g. common cold or influenza.
DERWENT CLASS: B02 B05
INVENTOR(S): LIM, L; TAN, Y H
PATENT ASSIGNEE(S): (UYSI-N) NAT UNIV OF SINGAPORE; (TANY-I) TAN Y H
COUNTRY COUNT: 7
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 396251	A	901107	(9045)*		
R: CH DE FR GB LI NL					
JP 03083933	A	910409	(9120)		
EP 396251	A3	920708	(9334)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 396251	A	EP 90-303361	900329
JP 03083933	A	JP 89-220144	890825
EP 396251	A3	EP 90-303361	900329

Searcher : Shears 308-4994

PRIORITY APPLN. INFO: GB 89-7308 890331; JP 89-220144 890825
AN 1990-336689 [45] WPIDS
AB EP 396251 A UPAB: 19931119
Specific cytokines are type I and II interferon. **Inhibition** of at least 50% is achieved. Compounds of use in thhis invention are monocarboxylic polyunsaturated fatty acids, their salts, 1-4C alkyl esters, amides and 1-4C alkylamides. Fatty acids have 14 to 24 carbon atoms most preferably 20. Suitable compounds include 5, 11, 14-eicosatetraenoic acid (arachidonic); 5, 8, 11, 14-eicosatetraynoic acid; 5,8,11-eicosatriynoic acid, linoleic acid and their derivatives. Other compounds are ketoconazole, **nordihydroguaiaretic** acid and quercetin. The compositions may be in the form of nasal drops, a nasal spray, a balm, cream or tablets. Dosage is 0.5 to 150 mg of arachidonic acid or analogue per dose when **administered** orally.

USE/ADVANTAGE - The compounds of the invention interfere with binding of ligands such as cytokines to cellular receptors and so **inhibit** the action of interferon on cells after an **antiviral** state has been established. They are therefore used to **treat viral** diseases especially the common cold or flu. @(17pp Dwg.No.0/7)
0/7

L37 ANSWER 50 OF 70 TOXLIT
ACCESSION NUMBER: 1991:31002 TOXLIT
DOCUMENT NUMBER: CA-114-115083U
TITLE: Use of fatty acids or other compounds for the **treatment** of diseases associated with cytokines, such as alleviation of symptoms of influenza or the common cold.
AUTHOR: Tan YH; Lim L
SOURCE: (1990). Eur. Pat. Appl. PATENT NO. 396251 11/07/90 (National University of Singapore).
PUB. COUNTRY: Singapore
DOCUMENT TYPE: Patent
FILE SEGMENT: CA
LANGUAGE: English
OTHER SOURCE: CA 114:115083
ENTRY MONTH: 199106
AB Arachidonic acid (I), an arachidonic acid analog, **nordihydroguaiaretic** acid (II), ketoconazole (III), or quercetin or used in the prepn. of a medicament for use in the **treatment** of a disease state assocd. with the endogenous presence and/or prodn. of a cytokine. The compds. of the invention can be used to alleviate the symptoms of the common cold or influenza. Thus, 50 muM I, 50 muM II, and 100 muM III **inhibited** the **antiviral** state induced by alpha- or

beta-interferon by .gtoreq.90%; 50 muM I also **inhibited** the **antiviral** state induced by gamma-interferon by .gtoreq.80%. Data are presented that suggest that I and other compds. of the invention can diminish the binding of ligands (interferon) to their receptors.

L37 ANSWER 51 OF 70 TOXLINE
ACCESSION NUMBER: 1991:13243 TOXLINE
DOCUMENT NUMBER: BIOSIS-91-00245
TITLE: Staphylococcal enterotoxin A induced interferon (IFN)-gamma production in spleen cells from BCG-immunized mice: The IFN production is dependent on leukotriene C4 but not dependent on interleukin 2.
AUTHOR: KATO K; SHIROSITA K; KUROSAWA S; MIZUKOSHI N; YAMAMOTO K-I; AZUMA I; OKUYAMA H; NISHIHIRA J
CORPORATE SOURCE: Dep. Intern. Med., Tomakomai City General Hosp., 1-2-21 Honkou-chyo, Tomakomai 053, Japan.
SOURCE: IMMUNOBIOLOGY, (1990). Vol. 181, No. 1, pp. 40-50. CODEN: IMMND4.
FILE SEGMENT: BIOSIS
LANGUAGE: English
ENTRY MONTH: 199102
AB BIOSIS COPYRIGHT: BIOL ABS. In our previous paper, we showed that IFN was induced in sera by injection of staphylococcal enterotoxin A (SEA) in Bacillus Calmette-Guerin (BCG) immmunized C57BL/6 (B6) mice. In analyzing the phenomenon in vitro, we showed that SEA induced IFN-gamma in the supernatant of the spleen cell culture from BCG immunized B6 mice and that leukotriene C4 (LTC4) from BCG activated macrophages in the spleen was involved in the IFN production from Ly 1+ T cells. On the other hand, interleukin-2 (IL-2) has reported to play an important role in the regulation of synthesis of IFn-gamma by T cells. In the present study, we examined whether IL-2 is involved in SEA-induced IFN production. The result showed that the SEA-induced IFN-gamma production was observed in spite of **suppression** of SEA-induced IL-2 production in spleen cells from BCG-immunized B6 mice. On the contrary, the depressed IFN production was observed in spite of high SEA-induced IL-2 production in spleen cells from their control mice. On other hand, LTC4 production was 8 times higher in spleen cells from BCG-immunized B6 mice, high producer of SEA-induced IFN, than in that from BCG-immunized C3H mice, the low producer. We also observed that the IFN and the LTC4 production of spleen cells from BCG-immunized B6 mice was **suppressed** in the presence of caffeic acid and **nordihydroguaiaretic** acid, non-specific lipoxygenase **inhibitors**, and that LTC4 augmented the IFN production of normal B6 mouse spleen cells in the presence of 2-mercaptoethanol. Therefore, involvement of LTC4 rather than of IL-2 was supported in our experimental system.

L37 ANSWER 52 OF 70 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 90002927 MEDLINE
DOCUMENT NUMBER: 90002927
TITLE: Mechanism of selective killing by dilinoleoylglycerol of cells transformed by the E1A gene of adenovirus type 12.
AUTHOR: Matsuzaki A; Shimura H; Okuda A; Ohtsu M; Sasaki M; Onodera K; Kimura G
CORPORATE SOURCE: Department of Virology, Kyushu University, Fukuoka, Japan.
SOURCE: CANCER RESEARCH, (1989 Oct 15) 49 (20) 5702-7.
Journal code: CNF. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199001
AB Rat 3Y1 fibroblasts transformed by the E1A gene of adenovirus type 12 (E1A-3Y1 cells) are highly sensitive to the cell-killing effect of 1,3-dilinoleoylglycerol (DLG) **administered** in a culture medium, whereas the parental 3Y1 cells are less sensitive (H. Shimura et al., Cancer Res., 48: 578-583, 1988). The selective cytotoxicity of DLG to E1A-3Y1 cells was markedly reduced by the simultaneous **administration** of nonspecific antioxidants such as vitamin E, butylated hydroxytoluene, and ascorbic acid. Specific scavengers for oxygen radicals had no effect. Lipoxygenase **inhibitors** (**nordihydroguaiaretic** acid, esculetin, and baicalein) reduced the DLG-mediated selective cytotoxicity, whereas cyclooxygenase **inhibitors** (acetylsalicylic acid and indomethacin) showed no effect. The intracellular and extracellular contents of the products from lipid peroxidation as measured by the thiobarbituric acid test were significantly greater in E1A-3Y1 cells than in the parental 3Y1 cells. In comparison with DLG, linoleic acid and monolinoleoylglycerol were equally toxic to E1A-3Y1 and parental 3Y1, and trilinoleoylglycerol was weakly toxic to both types of cells. Scanning electron microscopy revealed that numerous holes about 0.2 micron in diameter were scattered all over the surface of the E1A-3Y1 cells after **treating** the cultures with DLG. These results suggest that; (a) the DLG-mediated cytotoxicity to the E1A-transformed cells is attributable to lipid peroxidation; (b) the structural property of DLG is essential to the E1A specificity of cytotoxicity; and finally (c) the destruction of the cell membrane is the basis of cytotoxicity of DLG.

L37 ANSWER 53 OF 70 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 89-44753 DRUGU T P
TITLE: Phytohemagglutinin Mitogenic Response of Normal Individuals Vaccinated with Hepatitis B Vaccine.
AUTHOR: Filion L G; Saginur R; Izaguirre C A
Searcher : Shears 308-4994

LOCATION: Ottawa, Ontario, Canada
SOURCE: J.Infect.Dis. (160, No. 3, 398-404, 1989) 4 Fig. 3 Tab. 15 Ref.
CODEN: JIDIAQ ISSN: 0022-1899
AVAIL. OF DOC.: Department of Microbiology and Immunology, Faculty of Medicine, University of Ottawa, Ontario, K1H 8M5, Canada.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 89-44753 DRUGU T P
AB In 34 healthy people vaccinated i.m. with Hepatitis-B-vaccine (Heptavax B, HB, Merck-Frosst), the PHA response was **suppressed** 2 day after the first dose but not after subsequent doses. The PHA blastogenic response on day 7 was not enhanced by interleukin-2 (IL-2, Genzyme, USA) or indometacin (IN, Sigma-Chem.) though more cells expressed CD25 in their presence. Removal of CD4+ or CD8+ cells enhanced the PHA response on days 2 and 4 only. Addition of IL-2 alone or with PHA did not reverse the **suppression** at any time tested. In vitro **suppressor** cell induction was blocked by addition of IN at the time of culture initiation. Addition of IN or **nordihydroguaiaretate** to control cultures did not affect their response to PHA.

ABEX Methods The 13 males (mean age 30 yr, range 22-50 yr) and 21 females (mean age 27 yr, range 22-40 yr) were injected with 20 ug of HB in the deltoid muscle on days 0, 28 and 180. Results The blastogenic response to PHA was **suppressed** by about 33% on day 2 after vaccination but recovered by day 21. There was a significant increase in CD25 levels after the first HB dose which peaked on day 21. CD25 levels were significantly increased after each subsequent vaccination, reaching a maximum of 14% of peripheral blood mononuclear cells by day 187. The PHA response was boosted about 2-fold by the elimination of CD4+ or CD8+ cells from donors on days 2 and 4. At all other sampling times, the removal of these lymphocytes and especially CD4+ cells decreased the PHA blastogenic response. In vitro, cells needed to be incubated with HB for 3 days or more before stimulation with PHA in order to achieve effective **suppression** of the blastogenic response. (W137/LJ)

L37 ANSWER 54 OF 70 MEDLINE DUPLICATE 17
ACCESSION NUMBER: 89198836 MEDLINE
DOCUMENT NUMBER: 89198836
TITLE: Reversal of **virus**-induced alveolar macrophage bactericidal dysfunction by cyclooxygenase **inhibition** in vitro.
AUTHOR: Laegreid W W; Liggitt H D; Silflow R M; Evermann J R;

Taylor S M; Leid R W
CORPORATE SOURCE: Department of Veterinary Microbiology, Washington State University, Pullman 99164-7040.
SOURCE: JOURNAL OF LEUKOCYTE BIOLOGY, (1989 Apr) 45 (4) 293-300.
Journal code: IWY. ISSN: 0741-5400.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198907
AB **Virus** infection of alveolar macrophages (AM) both in vivo and in vitro has been associated with a decreased ability of these cells to kill bacteria, together with enhanced production of metabolites of arachidonic acid. These metabolites, especially PGE2, may be **inhibitory** to some phagocyte functions. Primary cultures of bovine AM obtained by bronchoalveolar lavage of normal cattle were infected in vitro with parainfluenza-3 (PI3 **virus**) **virus**. Killing of Staphylococcus epidermidis by AM was determined on days 1-4 post-infection (p.i.) PI3 **virus**-infected AM killed significantly fewer bacteria on day 4 p.i. compared to uninfected controls (12.1 +/- 1.3% infected vs. 52.7 +/- 7.2% controls, P less than or equal to 0.05). Bacterial killing by **virus**-infected AM, but not control AM, was significantly enhanced on day 4 p.i. by addition of cyclooxygenase **inhibitors** 1 hr prior to bactericidal assay (28.0 +/- 4.5% indomethacin, 36.0 +/- 4.1% mefenamic acid, 38.6 +/- 7.3% piroxicam, 37.0 +/- 6.4% **NDGA**, 44.9 +/- 7.7% ETYA, P less than or equal to 0.05). Phagocytosis of opsonized sheep erythrocytes and superoxide generation by **virus**-infected AM were not significantly increased by cyclooxygenase **inhibition**. Phagosome-lysosome fusion was severely impaired in **virus**-infected AM. Pretreatment of **virus** -infected AM with indomethacin significantly enhanced the percentage of cell expressing fusion activity. This data suggests that in vitro bactericidal dysfunction associated with **virus** infection of AM is partially the result of enhanced production of prostaglandins or thromboxane by AM and/or an abnormal response to normal levels of endogenously produced cyclooxygenase metabolites. The data further indicate the presence of cyclooxygenase sensitive (phagosome-lysosome fusion) and insensitive (phagocytic) components of **virus**-induced bactericidal dysfunction in AM.

L37 ANSWER 55 OF 70 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 89-15254 DRUGU T E
TITLE: Topical **Nordihydroguaiaretic** Acid (**NDGA**) in Psoriasis.
AUTHOR: Newton J A; Boodle K M; Barr R; Dowd P M; Greaves M W
LOCATION: London, United Kingdom
Searcher : Shears 308-4994

SOURCE: Br.J.Dermatol. (120, No. 2, 286-87, 1989) 1 Tab. 3 Ref.
CODEN: BJDEAZ ISSN: 0366-2845
AVAIL. OF DOC.: Institute of Dermatology, UMDS Guy's and St. Thomas', Lisle St, London WC2, England.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 89-15254 DRUGU T E
AB The clinical and pharmacological effects of **NDGA** applied topically were evaluated in 10 patients with stable plaque psoriasis. No clinical response was observed and no effect on LTB4 production was demonstrated by a chemokinesis bioassay or HPLC. A positive control **treated** with 0.025% betamethasone 17-valerate (BM) responded to **treatment**. (congress abstract).
ABEX 4 Patients with stable plaque psoriasis were initially studied. **NDGA** was applied topically using a limiting grid for 14 days. The **NDGA** was applied in methylated spirit in concentrations ranging from 0.5%-3%. No clinical effect of **NDGA** was seen although a positive control **treated** simultaneously with 0.025% BM ointment responded to **treatment**. A further 6 patients with psoriasis were, therefore, recruited. A large plaque was selected. Diameter circles of 3 x 2 cm were marked, each at least 4 cm apart. The 1st was left untreated, the 2nd was **treated** daily with a 3% solution (100 ul solution) of **NDGA** in methylated spirit under occlusion and the 3rd was **treated** identically, with solvent alone. 1 Patient was withdrawn at 5 days because she developed a **viral** infection. In the other 5, the clinical response was assessed and chamber fluid was collected after abrasion for the assay of LTB4 using HPLC and a chemokinesis assay. Again, no clinical response was demonstrated. Levels of LTB4/chamber were: 28 +/- 11, 22 +/- 8 and 19 +/- 8 pg in **NDGA**-, solvent- and untreated skin. (E54/RSV)

L37 ANSWER 56 OF 70 PROMT COPYRIGHT 1999 IAC

ACCESSION NUMBER: 90:463861 PROMT
TITLE: Chemex Pharmaceuticals - Research & Development Outlays
SOURCE: Annual Report, (1989) pp. 0.
LANGUAGE: English
AB 4. Yale University-The Company has two research contracts with the Yale University Department of Dermatology. Due to financial constraints, the Company has notified the University that it will terminate the general research contract at the end of the termination notice period, September 30, 1990. Chemex will continue to fund the Yale research contract for the development of

Oligonucleotide Directed Photochemotherapy. ONDP technology was discovered by Yale in 1988 and is owned by Chemex. The ONDP procedure, for which patents have been applied, is being investigated as a potential new **treatment** of inflammatory, immune and **viral** skin diseases. The termination of one of the two Yale contracts will reduce by one-half the Company's Yale research costs after September 30, 1990. 5. Other Projects-In addition to projects discussed above, financial resources permitting, the Company will advance development work on methotrezate, cytarabine, and CHX 108 for the potential **treatment** of psoriasis, **viral** warts, and dermatitis, respectively.
6. Withdrawal of INDs-For business and/or scientific reasons, Chemex has decided to suspend further development work on the following projects and has withdrawn relevant IND filings on these compounds only for the following potential **treatments**: **NDGA** (CHX 100) for psoriasis; spectinomycin (CHX 3101) for acne; amlexanox (CHX 3673) for psoriasis; propoxytane (CHX 107) for psoriasis; and CHX 3988 (Takeda PAF antagonist) for eczema.

L37 ANSWER 57 OF 70 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1988-161515 [23] WPIDS
DOC. NO. CPI: C88-072034
TITLE: Antitumour compsn. contg. organic cpd. e.g. 1,4-di phenyl-butane deriv - esp. with metal salt potentiator such as zinc chloride, also with antimicrobial and other activities.
DERWENT CLASS: B05 C03
INVENTOR(S): ALLEN, L M; JORDAN, R T
PATENT ASSIGNEE(S): (CHEM-N) CHEMEX PHARM INC
COUNTRY COUNT: 19
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8803805	A	880602	(8823)*	EN	130
RW: AT BE CH DE FR GB IT LU NL SE					
W: AU DK FI JP KP KR NO SU					
AU 8767794	A	880616	(8836)		
EP 290442	A	881117	(8846)	EN	
R: AT BE CH DE FR GB IT LI LU NL SE					
JP 01501791 W		890622	(8931)		
AU 9168662	A	910314	(9118)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8803805	A	WO 86-US2547	861119

Searcher : Shears 308-4994

EP 290442 A EP 86-900420 861119
JP 01501791 W JP 86-500359 861119

PRIORITY APPLN. INFO: WO 86-US2547 861119
AN 1988-161515 [23] WPIDS
AB WO 8803805 A UPAB: 19930923
Antitumour compsns. contain (1) a metal salt potentiator and (2) an organic component. Alternatively, they may contain only certain of the organic components, i.e. 3- or 4-tert.butylphenol; p-hydroxycinnamic acid; norisoguaiacin; d,l-**nordihydroguaiaretic** acid (**NDGA**); 1-(3,4-diacetoxyphenyl)- 4-phenylbuta-1,3-diene; 1,4-bis(3,4-dihydroxyphenethyl) benzene; alpha,omega-(7-14C)dicarboxylic acids or their salts.

The compsns. pref. contain a salt of Zn, Cr (III), Y, Co (II), Co (III), Ni, Mg, Al, Cu (I), Cu (II), Fe (III), Cd, Sb, Hg, Rb, V or other rare earth metals, and a typical organic cpd. is a catechol butane of formula (I). R1 and R2 = H; 1-12C alkyl, alkenyl, alkoxy or alkenyloxy; (CO)n(CH2)m(CO2)pRa; glycoside residues (opt. with hydroxy H replaced by 1-2C alkyl or (sic)alkoxy) or together are CH2; n and p = 0 or 1; m = 1-4; each Ra = H, or 1-12C alkyl or alkenyl; R7, R8 and R9 = H, O (sic), OR1 or two on adjacent C can be CH2; R3 and R4 = H, Me, Et, CHO or COOH; R5 and R6 = H, OH, OMe or O (sic).

USE/ADVANTAGE - The compsns. are used to **treat** a wide range of tumours, esp. adenocarcinoma of the breast. They are also useful for **treating** bacterial, **viral** and fungal infections; to debride selectively skin ulcers; and to heal lesions, acne, warts and inflammatory disorders. These compsns. are less toxic and more effective than the individual components.
0/0

L37 ANSWER 58 OF 70 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1988-133139 [19] WPIDS
CROSS REFERENCE: 88-292467 [41]; 89-008978 [02]
DOC. NO. CPI: C88-059576
TITLE: Compsns. of catecholic butane derivs. with zinc ions - for **treating** tumours and skin disorders.
DERWENT CLASS: B05
INVENTOR(S): JORDAN, R T
PATENT ASSIGNEE(S): (CHEM-N) CHEMEX PHARM INC
COUNTRY COUNT: 19
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8803026	A	880505	(8819)*	EN	50

Searcher : Shears 308-4994

RW: AT BE CH DE FR GB IT LU NL SE
W: AU DK JP KP KR NO SU
AU 8781724 A 880520 (8833)
EP 288534 A 881102 (8844) EN
R: AT BE CH DE FR GB IT LI LU NL SE
JP 01501794 W 890622 (8931)
US 4880637 A 891114 (9004) 13
EP 288534 B 911218 (9151)
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3775387 G 920130 (9206)
EP 288534 A4 890412 (9348)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8803026	A	WO 87-US2868	871027
EP 288534	A	EP 87-907401	871027
JP 01501794	W	JP 87-506947	871027
US 4880637	A	US 86-925620	861028
EP 288534	A4	EP 87-907401	

PRIORITY APPLN. INFO: US 79-49886 790619; US 82-365781 820405; US 83-465631 830210; US 84-578501 840409; US 85-699923 850211; US 86-924620 861028

AN 1988-133139 [19] WPIDS

CR 88-292467 [41]; 89-008978 [02]

AB WO 8803026 A UPAB: 19940223

Compsn. contg. ionic zinc (II) and at least one catecholic butane of formula (I). R1, R2 = H, lower alkyl, lower acyl; R3, R4, R5, R6, R10, R11, R12, R13 = H or lower alkyl; R7, R8, R9 = H, OH, lower alkoxy or lower acyloxy. More specifically the ionic zinc is in the form of a chelate or a salt, esp. ZnCl2 and (I) is nordihydroguairetic acid (**NDGA**). The molar ratio of (I):(II) is in the range 10:1 to 1:20.

USE/ADVANTAGE - The compsn. can be used for **treating** skin disorders such as solid tumours (both benign and malignant), acne, psariasis, wounds and infections (**viral**, bacterial and fungal). It does not cause the discomfort of zinc chloride alone or have the side effects of normal anticancer chemotherapy. Specific tumours for which the compsn. is partic. effective include mouse sarcoma-180, malignatn melanoma, human sarcoma-180, squamous cell carcinoma, lung squamous cell carcinoma, breast adenocarcinoma, glioma, glioastrocytoma, renal cell carcinome, Bowenoid carcinoma and basal cell carcinoma.

Dwg.0/0

ABEQ EP 288534 B UPAB: 19930923

A pharmaceutical composition characterised by comprising at least

one catecholic butane of the formula (I) wherein R1 and R2 are each independently H, C1-C6 alkyl or C1-C6 acyl; R3, R4, R5, R6, R10, R11, R12 and R13 are each independently H or C1-C6 alkyl; and R7, R8 and R9 are each independently H, hydroxy, C1-C6 alkoxy or C1-C6 acyloxy; and ionic zinc.

ABEQ US 4880637 A UPAB: 19930923

New pharmaceutical compsns. comprise at least 1 catecholic butane of formula (II) and ionic Zn. In (I), R1 and R2 are each H,1-6Calkyl or acyl; R3-R6 and R10-R13 are each H, 1-6Calkyl: R7-R9 are each H,OH,1-6C-alkoxy or -acyloxy. Pref. ionic Zn is as Zn salt or chelate of catecholic butane of mol ratio 1:1 to 1:20. Pref. catecholic butane is **nordihydroguaiaretic** acid of formula (I).

USE/ADVANTAGE - **Treatment** of benign, premalignant and malignant solid tumours, esp. of skin. Dose 2-20 mg/ch2 solid tumour.

ABEQ EP 288534 A UPAB: 19940120

Compsn. contg. ionic zinc (II) and at least one catecholic butane of formula (I). R1, R2 = H, lower alkyl, lower acyl; R3, R4, R5, R6, R10, R11, R12, R13 = H or lower alkyl; R7, R8, R9 = H, OH, lower alkoxy or lower acyloxy. More specifically the ionic zinc is in the form of a chelate or a salt, esp. ZnCl2 and (I) is nordihydroguairetic acid (**NDGA**). The molar ratio of (I):(II) is in the range 10:1 to 1:20.

USE/ADVANTAGE - The compsn. can be used for **treating** skin disorders such as solid tumours (both benign and malignant), acne, psariasis, wounds and infections (**viral**, bacterial and fungal). It does not cause the discomfort of zinc chloride alone or have the side effects of normal anticancer chemotherapy. Specific tumours for which the compsn. is partic. effective include mouse sarcoma-180, malignatn melanoma, human sarcoma-180, squamous cell carcinoma, lung squamous cell carcinoma, breast adenocarcinoma, glioma, glioastrocytoma, renal cell carcinome, Bowenoid carcinoma and basal cell carcinoma.

L37 ANSWER 59 OF 70 TOXLIT

ACCESSION NUMBER: 1989:38544 TOXLIT
DOCUMENT NUMBER: CA-110-141554K
TITLE: Pharmacologically active compositions of catecholic butanes with zinc for treatment of skin diseases.
AUTHOR: Jordan RT; Allen LM
SOURCE: (1988). PCT Int. Appl. PATENT NO. 88 01509 03/10/88 (Chemex Pharmaceuticals, Inc.).
PUB. COUNTRY: United States
DOCUMENT TYPE: Patent
FILE SEGMENT: CA
LANGUAGE: English
OTHER SOURCE: CA 110:141554
ENTRY MONTH: 198905

AB Catecholic butanes I (R1, R2 = alkyl, acyl; R3, R4 = H, Me, Et; R5, R6 = H, OH; R7, R8, R9 = H, OH, OR1) as Zn salts or chelates, or I mixts. with Zn salts, are drugs for the treatment of skin diseases, esp. fungal or bacterial diseases and cancer. A mixt. of ZnCl2 46, meso-1,4-**bis**(3,4-**dihydroxyphenyl**)-2,3-**dimethylbutane** 11.5, quercetin 11.5, Na ascorbate 7.7, solvent 3.0, and polyethylene glycol 20.4% by wt., applied topically twice, controlled B-16 melanoma and S-180 tumor, in mice.

L37 ANSWER 60 OF 70 MEDLINE DUPLICATE 18
ACCESSION NUMBER: 87160921 MEDLINE
DOCUMENT NUMBER: 87160921
TITLE: The effect of modulating the synthesis of arachidonic acid cascade products on HSV lesion recurrence.
AUTHOR: Yates F; Centifanto Y M; Caldwell D R
SOURCE: CURRENT EYE RESEARCH, (1987 Jan) 6 (1) 99-104.
Journal code: DUB. ISSN: 0271-3683.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English.
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198707

AB Induction of HSV lesion recurrence may be achieved by a variety of stimuli. Trauma of almost any kind (physical, chemical, electromagnetic and thermal) to the healed primary lesion site has been successful for induction of recurrence. In common with each of these mechanisms is the release of inflammatory mediators (arachidonic acid (AA), complement, kinins, etc.) following trauma. Because blockade of the AA cascade with steroids has been noted to abort HSV skin lesions, and because steroids have numerous side effects making them a poor **therapeutic** choice in ocular lesions, we decided to test several relatively different types of AA cascade **inhibitory** drugs in mouse ear HSV recurrence models. In this series of experiments, it was found that topical steroids gave the greatest initial decrease in lesion number (80% fewer than control on day 3 post recurrence induction (PRI), while meclofenamate resulted in the greatest reduction of lesions by day 5 PRI (85% fewer lesions than control and 60% fewer than the steroid **treated** group). The **NDGA treated** group exhibited the least reduction in recurrence severity (27% fewer lesions than control on day 5 PRI and 200% more lesions than the steroid group. Chlorpromazine (thorazine) acted roughly equivalent to the steroid **treated** group by day 5 PRI (70% fewer lesions than the untreated control group). Relative efficacy in lesion reduction between groups by day 5 PRI is: meclofenamate greater than steroid = chlorpromazine greater than **NDGA** greater than control. Meclofenamate, steroid and chlorpromazine significantly reduced lesions (p less than .05) when compared with the saline **treated** control mice. **NDGA** did not

significantly reduce lesions by day 5 PRI.

L37 ANSWER 61 OF 70 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1986-318726 [48] WPIDS
DOC. NO. CPI: C86-138033
TITLE: Reducing trans-dermal flux of anti neoplastic agent - by addn. of water-soluble zinc cpd., esp. zinc chloride, to enhance skin retention.
DERWENT CLASS: B07
INVENTOR(S): ALLEN, L M
PATENT ASSIGNEE(S): (CHEM-N) CHEMEX PHARM INC; (ACCE-N) ACCESS PHARM INC
COUNTRY COUNT: 17
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8606586	A	861120	(8648)*	EN	40
RW: AT BE CH DE FR GB IT LU NL SE					
W: AU DE DK FI GB JP NO					
AU 8659066	A	861204	(8718)		
EP 221176	A	870513	(8719)	EN	
R: AT BE CH DE FR GB IT LI LU NL SE					
NO 8700001	A	870406	(8720)		
FI 8700013	A	870102	(8740)		
DK 8606349	A	870202	(8751)		
JP 63500171	W	880121	(8809)		
US 4895727	A	900123	(9011)		
AU 9055883	A	900913	(9044)		
EP 506207	A2	920930	(9240)	EN	19
R: AT BE CH DE FR GB IT LI LU NL SE					
EP 506207	A3	930303	(9349)		
EP 221176	B1	940914	(9435)	EN	18
R: AT BE CH DE FR GB IT LI LU NL SE					
DE 3650068	G	941020	(9441)		
EP 872248	A2	981021	(9846)	EN	
R: AT BE CH DE FR GB IT LI LU NL SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8606586	A	WO 86-US974	860502
EP 221176	A	EP 86-903757	860502
JP 63500171	W	JP 86-502882	860502
US 4895727	A	US 85-730682	850503
EP 506207	A2	EP 92-201393	860502
EP 506207	A3	EP 92-201393	860502
EP 221176	B1	EP 86-903757	860502

Searcher : Shears 308-4994

		WO 86-US974	860502
DE 3650068	G	DE 86-3650068	860502
		EP 86-903757	860502
		WO 86-US974	860502
EP 872248	A2 Div ex	EP 86-903757	860502
	Div ex	EP 92-201393	860502
		EP 98-105208	860502

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 506207	A2 Related to	EP 221176
EP 221176	B1 Based on	WO 8606586
DE 3650068	G Based on	EP 221176
	Based on	WO 8606586
EP 872248	A2 Div ex	EP 221176
	Div ex	EP 506207

PRIORITY APPLN. INFO: US 85-730682 850503

AN 1986-318726 [48] WPIDS

AB WO 8606586 A UPAB: 19930922

Additional cites.:- US4122170 US3989816 US3991203 US4411893 US4199576 US41488US4148874 US4362745

Enhancement skin and mucous membrane retention of a pharmacologically active agent (I) comprises adding to (I) a water-soluble Zn cpd., pref. ZnCl2. (I) is VP-16 (epipodophyllotoxin beta-D ethylidene glucopyranoside-etoposide) VM-26 (epipodophyllotoxin beta-D thenylidene glucopyranoside-teniposide), 4'-demethyl-epipodophyllotoxin, diethylstilbestrol, dithranol, cyclophosphamide, mitomycin, daunomycin, platinum cis-diamine-dichloride, adriamycin or allopurinol.

USE/ADVANTAGE - Retention in the skin is enhanced and prolonged, maximising topical **therapeutic** effects of pharmaceutical and cosmetic agents and reducing systemic effects of those agents which have systemic activity or toxicity. The specified agents (I) are antineoplastic agents, but the method is more widely applicable e.g. to immunopharmacological agents, antiinflammatory or anti pruritic steroids, topical antifungals, antibacterials or **antivirals**, antiparasitics, e.g. anthelmintics, pediculicides, anti-acne agents, antipsoriatics, antileprotics, topical anaesthetics, analgesics, counter-irritants, antihistamines, diagnostic agents, vitamins, cosmetic agents and sunscreens.

ABEQ US 4895727 A UPAB: 19930922

Penetration of skin and mucous membrane by a pharmacologically active agent is enhanced and retained, by applying a water-soluble Zn-contg. cpd. which acts to reduce transdermal flux of the agent.

Zn-contg. cpd. comprises ZnCle,ZnSO4,Zn(NO3)2, zinc acetate, or zinc stearate. Pharmacological agent comprisese e.g. steroid,

antiparasitic agent, antileprosy agent, antimetabolite, cell-regulatory agent, immuno-pharmacological agent, allergen, antihistaminic agent, antiinflammatory agent, etc.

ADVANTAGE - Drugs are absorbed and retained for longer periods, overcoming and reducing undesirable systemic toxicity.

ABEQ EP 506207 A UPAB: 19940126

Additional citns.:- US4122170 US3989816 US3991203 US4411893 US4199576 US41488US4148874 US4362745

Enhancement skin and mucous membrane retention of a pharmacologically active agent (I) comprises adding to (I) a water-soluble Zn cpd., pref. ZnCl2. (I) is VP-16 (epipodophyllotoxin beta-D ethylidene glucopyranoside-etoposide) VM-26 (epipodophyllotoxin beta-D thenylidene glucopyranoside-teniposide), 4'-demethyl-epipodophyllotoxin, diethylstilbestrol, dithranol, cyclophosphamide, mitomycin, daunomycin, platinum cis-diamine-dichloride, adriamycin or allopurinol.

USE/ADVANTAGE - Retention in the skin is enhanced and prolonged, maximising topical **therapeutic** effects of pharmaceutical and cosmetic agents and reducing systemic effects of those agents which have systemic activity or toxicity. The specified agents (I) are antineoplastic agents, but the method is more widely applicable e.g. to immunopharmacological agents, antiinflammatory or anti pruritic steroids, topical antifungals, antibacterials or **antivirals**, antiparasitics, e.g. anthelmintics, pediculicides, anti-acne agents, antipsoriatics, antileprotics, topical anaesthetics, analgesics, counter-irritants, antihistamines, diagnostic agents, vitamins, cosmetic agents and sunscreens.

ABEQ EP 221176 B UPAB: 19941021

A topical pharmaceutical composition for application to the skin or mucous membrane having enhanced skin and mucous membrane penetration and retention comprising a pharmaceutically active agent and an effective amount of a water-soluble zinc-containing compound wherein the pharmacologically active agent is VP-16 (epipodophyllotoxin beta-D ethylidene glucopyranoside-etoposide); VM-26 (epipodophyllotoxin beta-D thenylidene glucopyranoside- teniposide); 4'-demethyl epipodophyllotoxin; diethylstilbestrol; dithranol; cyclophosphamide; mitomycin; daunomycin; platinum cis-diamine-dichloride; adriamycin; allopurinol; 5-fluorouracil, methotrexate or **NDGA** (**nordihydroguaiaretic** acid).

Dwg.0/1

L37 ANSWER 62 OF 70 MEDLINE

ACCESSION NUMBER: 87002662 MEDLINE

DOCUMENT NUMBER: 87002662

TITLE: Effects of **inhibitors** of arachidonic acid metabolism on intercellular adhesion of SV40-3T3 cells.

AUTHOR: Evans P M; Lanham D F

Searcher : Shears 308-4994

SOURCE: CELL BIOLOGY INTERNATIONAL REPORTS, (1986 Sep) 10 (9) 693-8.
Journal code: CRC. ISSN: 0309-1651.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198701

AB Mepacrine, an **inhibitor** of arachidonic acid mobilisation, and **NDGA**, a lipoxygenase **inhibitor**, were found to impair the aggregation of SV40-3T3 cells but the effects could not be unequivocally dissociated from non-specific actions of the drugs. No effect on aggregation was observed even after prolonged exposure of the cells to the cyclooxygenase **inhibitors** aspirin and indomethacin. These results argue against a possible regulatory role for endogenous AA metabolites in intercellular adhesion of SV40-3T3 cells.

L37 ANSWER 63 OF 70 MEDLINE DUPLICATE 19
ACCESSION NUMBER: 87002016 MEDLINE
DOCUMENT NUMBER: 87002016
TITLE: **Inhibition** of 12-O-tetradecanoylphorbol-13-acetate-induced induction of Epstein-Barr **virus** early antigen in Raji cells by some **inhibitors** of tumor promotion.
AUTHOR: Saito Y; Okamoto H; Mizusaki S; Yoshida D
SOURCE: CANCER LETTERS, (1986 Aug) 32 (2) 137-44.
Journal code: CMX. ISSN: 0304-3835.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198701

AB The effects of some compounds, which have been reported to **inhibit** tumor promotion in vivo, on the induction of the early antigen (EA) of Epstein-Barr **virus** (EBV) by 12-O-tetradecanoylphorbol-13-acetate (TPA) in Raji cells were examined. The **inhibitors** of the cascade process involving arachidonic acid, indomethacin, **nordihydroguaiaretic** acid, phenidone and p-bromophenacyl bromide, effectively **inhibited** EBV-EA induction by TPA. Two flavonoids, morin and kaempferol also **inhibited** EA induction. Among antioxidants, butylated hydroxytoluene effectively **inhibited** EA induction, though alpha-tocopherol did not show any **inhibition** of EA induction at concentrations of up to 150 micrograms/ml. N-(6-Aminohexyl)-5-chloro-1-naphthalenesulfonamide, a calmodulin antagonist, and esculetin showed **inhibitory** effects on EA induction, though slight cytotoxicity was observed. L-1-p-Tosylamino-2-phenylethyl chloromethyl ketone, a protease

inhibitor, showed cytotoxicity and no specific **inhibition** of EA induction. Five kinds of steroids, cortisone, hydrocortisone, prednisolone, dexamethasone and fluocinolone acetonide showed no **inhibitory** effect on EA induction at concentrations of up to 100 micrograms/ml. In addition, the relationship between the **inhibition** of EBV-EA induction and that of tumor promotion is discussed.

L37 ANSWER 64 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE 20

ACCESSION NUMBER: 86032323 EMBASE
DOCUMENT NUMBER: 1986032323
TITLE: Reversal of feline retroviral **suppression** by indomethacin.
AUTHOR: Lewis M.G.; Fertel R.H.; Olsen R.G.
CORPORATE SOURCE: Department of Veterinary Pathobiology, The Ohio State University Columbus, OH 43210, United States
SOURCE: Leukemia Research, (1985) 9/12 (1451-1456).
CODEN: LEREDD
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
016 Cancer
047 Virology
030 Pharmacology
026 Immunology, Serology and Transplantation
LANGUAGE: English

AB The immunosuppressive effect of feline leukemia **virus** (FeLV) and its 15,000 dalton envelope protein (p15E) were studied to determine if the mechanism of action was due to an increase in prostaglandin production. We examined the effects of exogenous PGE1 and PGE2 on the normal Con A response of feline peripheral blood lymphocytes (PBL) and found them to be **inhibitory**. The addition of the cyclooxygenase **inhibitor** indomethacin to cells incubated with FeLV or FeLV p15E and Con A completely abrogated the **viral suppressive** effects. This reversal was titratable and time-dependent. Other non-steroidal anti-inflammatory (NSAI) drugs were found to have similar actions. Indomethacin was also able to increase the **suppressed** Con A response of PBL from FeLV-infected cats. Upon measurement of PGE2 levels from PBL cultured with FeLV, we found a decrease in PGE2 accumulation associated with FeLV presence during the first 24 h of culture. These findings indicate that FeLV does not cause its immunosuppressive effects by increasing PG production and suggests that indomethacin and the other tested NSAI drugs do not produce their effect by PG **inhibition**.

L37 ANSWER 65 OF 70 MEDLINE
ACCESSION NUMBER: 85303524 MEDLINE
Searcher : Shears 308-4994

DOCUMENT NUMBER: 85303524
TITLE: The lipoxygenase pathway in the human NK cell system.
AUTHOR: Jondal M; Kullman C; Lindgren J A; Rossi P
SOURCE: ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1985) 184 257-70.
Journal code: 2LU. ISSN: 0065-2598.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198512

L37 ANSWER 66 OF 70 MEDLINE DUPLICATE 21
ACCESSION NUMBER: 85201742 MEDLINE
DOCUMENT NUMBER: 85201742
TITLE: Products of the lipoxygenase pathway in human natural killer cell cytotoxicity.
AUTHOR: Rossi P; Lindgren J A; Kullman C; Jondal M
SOURCE: CELLULAR IMMUNOLOGY, (1985 Jun) 93 (1) 1-8.
Journal code: CQ9. ISSN: 0008-8749.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198509
AB As earlier data suggested the importance of lipoxygenase activation for expression of human NK cell cytotoxicity, four different lipoxygenase **inhibitors** were tested for **suppression** of natural killer (NK) cell lysis. All **inhibitors** were found active at nontoxic concentrations with 50% **inhibition** at approximately 15 microM for **nordihydroguaiaretic** acid (**NDGA**). NK cell lysis could be reconstituted to **NDGA-suppressed** cells with leukotriene B4 (LTB4), the all-trans isomers 6-trans-LTB4 and 12-epi-6-trans-LTB4, and 20-COOH-LTB4. LTB4 reconstitution was best in the concentration range 1-100 pM and near control levels at both higher and lower concentrations. **Herpesvirus** Ateles-transformed killer T cells could also be **inhibited** by **NDGA**. These data indicate that lipoxygenase activity is required for human NK cell lysis and that several different LTB4-related products can restore NK activity in **inhibited** cells; they also suggest that the lipoxygenase pathway is present in the killer cell population.

L37 ANSWER 67 OF 70 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1985:4076 BIOSIS
DOCUMENT NUMBER: BR28:4076
TITLE: NATURAL CYTOTOXIC CELL ACTIVITY ENHANCED BY LEUKOTRIENE B-4 MODULATION BY CYCLOOXYGENASE AND

LIPOXYGENASE **INHIBITORS**.
AUTHOR(S): ROLA-PLESZCZYNSKI M; GAGNON L; SIROIS P
CORPORATE SOURCE: LAB. D'IMMUNOL., DEP. PEDIATRIE, FAC. MED., UNIV. SHERBROOKE, SHERBROOKE, QUEBEC, J1H 5N4 CAN.
SOURCE: THALER-DAO, H., A. CRASTES DE PAULET AND R. PAOLETTI (ED.). ICOSANOIDS AND CANCER; SATELLITE SYMPOSIUM OF THE 2ND INTERNATIONAL CONGRESS ON HORMONES AND CANCER, ILE DE BENDOR, SEPT. 1983. XIX+289P. RAVEN PRESS: NEW YORK, N.Y., USA. ILLUS, (1984) 0 (0), 235-242.
ISBN: 0-88167-019-7.
FILE SEGMENT: BR; OLD
LANGUAGE: English

L37 ANSWER 68 OF 70 MEDLINE DUPLICATE 22
ACCESSION NUMBER: 83256539 MEDLINE
DOCUMENT NUMBER: 83256539
TITLE: Leukotriene B4 augments human natural cytotoxic cell activity.
AUTHOR: Rola-Pleszczynski M; Gagnon L; Sirois P
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1983 Jun 15) 113 (2) 531-7.
Journal code: 9Y8. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198310
AB We have recently shown that leukotriene B4 (LTB4) activates T lymphocytes to become **suppressor** cells. We now report that LTB4 also augments human natural cytotoxic cell activity against target cells infected with **herpes** simplex **virus**. This activity is partially **inhibited** by the lipoxygenase **inhibitor nordihydroguaiaretic** acid and the thromboxane synthetase **inhibitor** OKY-1581, but is augmented by indomethacin. We suggest that LTB4 may play a role in early host defense responses during inflammatory and infectious disease processes.

L37 ANSWER 69 OF 70 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 83183311 EMBASE
DOCUMENT NUMBER: 1983183311
TITLE: Leukotriene B4 augments human natural cytotoxic cell activity.
AUTHOR: Rola Pleszczynski M.; Gagnon L.; Sirois P.
CORPORATE SOURCE: Lab. Immunol., Unite Rech. Pulm., Fac. Med., Univ. Sherbrooke, Que. J1H 5N4, Canada
SOURCE: Biochemical and Biophysical Research Communications, (1983) 113/2 (531-537).

CODEN: BBRCA
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
029 Clinical Biochemistry
026 Immunology, Serology and Transplantation
047 Virology
LANGUAGE: English

AB We have recently shown that leukotriene B4 (LTB4) activates T lymphocytes to become **suppressor** cells. We now report that LTB4 also augments human natural cytotoxic cell activity against target cells infected with **herpes** simplex **virus**. This activity is partially **inhibited** by the lipoxygenase **inhibitor nordihydroguaiaretic** acid and the thromboxane synthetase **inhibitor** OKY-1581, but is augmented by indomethacin. We suggest that LTB4 may play a role in early host defense responses during inflammatory and infectious disease processes.

L37 ANSWER 70 OF 70 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
ACCESSION NUMBER: 83-27628 DRUGU P B
TITLE: Mechanisms of Fever.
AUTHOR: Hellon R; Townsend Y
LOCATION: London, United Kingdom
SOURCE: Pharmacol.Ther. (19, No. 2, 211-44, /1982/1983/) 20 Fig. 3 Tab. 201 Ref.
CODEN: PHTHDT ISSN: 0163-7258
AVAIL. OF DOC.: National Institute for Medical Research, London, NW7, England.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 83-27628 DRUGU P B
AB The mechanisms of fever are reviewed with respect to endogenous pyrogens and their biosynthesis, metabolism, release and site of action, central mediators of fever, the fever response in pregnant and neonatal animals and the survival value of the fever response. Endogenous pyrogens appear to be proteins released by leukocytes with a site of action in the hypothalamus. Candidates for the central mediator of fever include prostaglandins, monamines and proteins.
ABEX Many clinical conditions can give rise to fever including bacterial, **viral**, protozoal, and fungal infections, malignancies, immunological diseases and inflammatory disorders. Endotoxins from gram negative bacteria induce a febrile response. However, gram positive bacteria and **viruses** do not have an endotoxin but induce the synthesis of an endogenous pyrogen (EP) by being phagocytosed. EP is derived from leukocytes, especially